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REPORT

BELLEVUE AND ALLIED HOSPITALS

OF

THE CITY OF NEW YORK

VOLUME II

1909-1910

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MEDICAL AND SURGICAL

REPORT

OF

Bellevue and Allied Hospitals

IN

THE CITY OF NEW YORK.

VOLUME IV.

1909-1910.

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A CONTRIBUTION TO THE NORMAL AND PATHOLOGICAL HISTOLOGY OF THE THYMUS GLAND.*

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I. INTRODUCTION—The thymus gland has been a puzzle to the histologist as well as to the physiologist. At the present time there is no agreement as to its finer structure, and the traditional conception of the thymus as a peculiar lymph gland distinguished only by the presence of typical epithelial inclusions known as Hassall's bodies is still handed down blindly from one text-book to another. It has seemed to the writer that a critical histological study of the thymus based upon recent valuable contributions to the literature, as well as fairly extensive personal observations, would be timely and of value in fixing our conception of the normal structure of this organ. The attempt has also been made to outline the pathology of the thymus upon the basis of a more rational interpretation of its normal structure. The writer fully realizes the many defects and omissions in this portion of his work, but it is hoped that the effort will revive interest in the subject and encourage further work in this comparatively unexplored corner of pathology.

II. MATERIAL AND TECHNIC—The material for this study was obtained at autopsy, usually within twenty-four hours after death, rarely as late as forty-eight hours. Since the work was undertaken primarily in connection with Dr. Norris'† study of status lymphaticus, the majority of thymuses studied were taken from subjects showing this condition to a greater or lesser degree. Sufficient normal cases, however, were studied to serve as controls.

The human embryonic material was, unfortunately, not abundant; the earliest thymus studied was from a three months' fetus, the thymus being preserved in picro-sublimate and cut in series. The material from later cases was more abundant, including four, five, seven, eight months, and full-term organs.

As a routine fixing agent, Zenker's solution was used, but occasionally formalin, Orth's fluid, Tellyesnicsky's fluid and Fleming's solution were employed as controls. Paraffine sections not exceeding 5μ were stained in most cases with polychrome methylene blue erosin, Heidenhain's iron hematoxylin, with or without picro-fusine counterstain. Mallory's phosphostungic hematoxylin and Mallory's aniline blue. The phosphostungstic stain proved especially serviceable for demonstrating the fibrillary structure of the reticulum and Hassall bodies, and the myoid cells. A few cases were also impregnated with silver after the method of Bielschowsky-Maresch, for the demonstration of the finer connective tissue fibrils.

A certain number of old celloidin sections stained with hematoxylin eosin were studied, but proved of little value in detecting the finer structural details.

III. THE HISTOGENESIS OF THE THYMUS—The origin of the thymus as a paired outgrowth from the entodermal epithelium of the third branchial clefts has been conclusively proven by the classical studies of Kölliker (1), His (2), Stieda (3), Born (4), Fischelis (5), Kastschenko (6), Bell (7), and Fox (8). Whether the ectodermal lining of the sinus precervicalis or outer portion of the branchial cleft contribute to the formation of the upper extremity of the gland, as Fischelis (5) and Kastschenko (6) maintain, is very questionable. It is certain that the major portion of the thymus in all classes of vertebrates is derived from the entodermal epithelium.

As to the changes which the thymus undergoes in its subsequent development, there has never been any agreement. Histologists have in the main been divided into two camps in regard to the manner in which the gland comes to assume its lymphoid appearance. The one party, represented by His (2), Stieda (3), Dohrn (9), and Gulland (10) believes that the original epithelial anlage soon becomes invaded by lymphocytes and blood vessels from the surrounding tissue. The subsequent

*Reprinted from the Journal of Medical Research, February, 1910, in which the plates that accompanied the original article can be seen.

† An abstract of this paper, which will appear shortly, was read at the meeting of the American Society of Pathologists and Bacteriologists in Boston, May, 1909.

proliferation of the lymphocytes in situ gives rise to the cortical portions of the lobules. The reticulum is also derived from the connective tissue through the ingrowth of mesenchymal elements into the lobules. In the fully developed thymus the Hassall bodies represent the sole rests of the original epithelial anlage.

This view has been known as the "transformation" theory, and is the one commonly reproduced in the textbooks.

The other party, under the leadership of Beard (11), fails to find evidence of lymphocytic immigration and believes that the "lymphoid" cells arise in situ through repeated division of the epithelial cells. Indeed, Beard, as a result of his studies upon Raja Batis, considers the thymus to be the chief source of supply for the fetal lymphocytes, and whereas few histologists have accepted this extreme view, the "metamorphosis" theory has had many notable adherents, amongst them Kölliker (1),* Nussbaum and Prymak (12), Prenant (13), Stöhr (14), Bell (7), and Marcus (15).

Ver Eecke (16), in his study of the frog's thymus reaches conclusions somewhat at variance with the "transformation" theory. The lymphocytes arise in the mesodermal tissue and invade the epithelial anlage; epithelial structures, corresponding to the Hassall bodies in the higher vertebrates, are, however, permanent functional elements. For the combined lymphoid and epithelial tissue, he suggests the term "lymphothelial."

Maurer (17) also occupies an intermediate position. In amphibians, he believes with Ver Eecke that the lymphocytes are mesenchymal in origin, and invade the gland secondarily, whereas in Teleosts and reptiles they are developed in situ from the epithelial cells.

The most important recent contributions to the histogenesis of the thymus cells are those of Hammar, Stöhr, and Bell. Since their work fundamentally controverts the previous views, it is necessary to consider their observations in some detail in so far as they relate to the origin of the various elements of the thymus.

Hammar (18) has studied the embryonic thymus in the Teleosts, reptiles, birds, and mammals. He finds that the original epithelial elements are represented throughout the functional life of the gland, forming the greater portion of the medullary substance, and frequently extending to the surface of the lobules. The first changes noted in the epithelial anlage are from a solid aggregation of cells to a looser arrangement, in which the individual cells give off irregular protoplasmic processes which anastomose to form a cellular reticulum. This is sharply limited against the adjacent connective tissue. The outer or peripheral cells (Randschicht) are often cylindrical and radially disposed. The continued rarefaction of the anastomosing epithelial cells give rise to a delicate syncytial reticulum, which acts as a supporting meshwork for the small thymus cells. The reticular cells, therefore, are not connective tissue cells, have not the power to form collagenous fibrils, and must be considered as important epithelial constituents of the organ.

The Hassall bodies represent further differentiation forms of the epithelial reticular cells, which tend to undergo regressive changes.

As regards the lymphoid cells, Hammar believes with the older writers that they are of mesodermal origin, invading the gland secondarily, and there undergoing further proliferation. He bases this view largely upon his observations on Teleost embryos. The egg of Syphonostoma after fertilization is carried by the male in a special breeding pouch. By removing eggs at twelve-hour intervals, Hammar obtained a complete series. At one stage of development, he describes and depicts an invasion of the epithelial lobules by lymphoid cells originating in the mesodermal tissue.

The drawing intended to illustrate the immigration of lymphocytes from the subthymic tissue into the lobules is, however, not altogether convincing. At the point of entrance there is a distinct laceration of the basement membrane, which could not be other than artificial. Furthermore, although Hammar distinctly denies the occurrence of transitional forms between the reticular epithelial cells and the small thymic cells, his plates show undoubted protoplasmic connections between the two kinds of cells.

Stöhr (14) in 1905, in a preliminary communication, announced his belief in the epithelial origin and nature of the small thymic cells, and in the following year published a very interesting and elaborate study in support of this view. He is in agreement with Hammar as regards the epithelial nature and mode of formation of the reticulum, but finds no conclusive evidence of lymphocytic invasion at any stage of development, and shows that the small cells are present in the thymus before they appear in the adjacent connective tissue. The small cells therefore arise in situ

* Kölliker, in his description, strongly emphasizes the epithelial origin of the "lymphoid" cells, although he realizes that this interpretation would violate the usual conception as to the specificity of the germinal layers.

from the repeated multiplication of the reticular epithelium, and though morphologically they come to assume a structure indistinguishable from that of the true lymphocytes, they remain throughout true epithelial elements.

Bell (7) in 1905 also contributed a careful study of the histogenesis of the thymus cells in pig embryos. He describes and illustrates the differentiation of the original epithelial anlage into reticular syncytium, transitional "lymphoblastic" forms still showing protoplasmic connections with the reticular epithelium, and free, fully-formed lymphocytes. The small thymic cells, however, though epithelial in origin, are true lymphocytes and, in the later stage of development, emigrate into the surrounding connective tissue. In favor of the latter contention, he cites the presence of lymphocytes in large numbers in the interlobular septa, but naturally is unable to give any evidence that such a migration of small thymic cells actually occurs. Nor can one exclude the possibility that these collections of small round cells in the connective tissue represent developing lymphoid nodules.

The present status of the question as to the nature of the small cells is therefore still unsettled, although the weight of evidence is strongly in favor of their epithelial genesis. The epithelial nature of the reticulum, on the other hand, may be taken as assured, since all the recent studies in which modern staining methods were employed are in accord in confirming this view. So far as the origin of the small thymic cells is concerned, my own studies support the view of Stöhr that they are developed in situ from the original epithelial cells. In the earliest human material examined, a well preserved nine-centimeter (three months) fetus, the thymic cells were already of two fairly distinct types, between which there were, however, numerous transitional forms. The smaller cells, corresponding to the so-called lymphoid cells, contained a well-stained spherical nucleus, with abundant chromatin granules, and usually a distinct eccentrically placed nucleolus. The scant ragged cytoplasm stained distinctly with eosin and frequently showed protoplasmic connections with the larger cells. The latter, for which we shall use the term reticular epithelium, are somewhat larger than the cells of the first type. Their nuclei are likewise spherical or oval, but stain less intensely with hematoxylin, and take a more purplish tinge with polychrome methylene blue. The chromatin granules are more scanty, irregular in shape and tend to lie against the nuclear membrane. The cytoplasm is relatively more abundant than that of the small cells. The cell outline is very indistinct, and the protoplasm drawn out into ragged processes anastomosing with those of similar neighboring cells.

Mitoses are not numerous and are found only in the periphery of the lobules.

The lobular masses of glandular tissue are separated by very loose connective tissue of the embryonic type containing pale elliptical or fusiform nuclei. The numerous blood vessels, which already penetrate the lobules, are closely packed with erythrocytes and moderate numbers of erythroblasts, but contain no lymphocytes. Neither are there any lymphocytes found lying free in the interlobular septa, nor along the course of the intralobular blood vessels.

It is evident, therefore, that at this stage of development where the differentiation into two types of cells is already established, no invasion of the gland by lymphocytes from the surrounding connective tissue is taking place.

In all the latter embryonic material examined, the same paucity of lymphoid cells in the stroma was observed, and never any appearance suggesting an immigration of lymphocytes into the lobules. It is plain, therefore, that if such an invasion of the epithelial lobules takes place, the process must be completed at the third month. Not having had an opportunity to examine earlier human material, I am hardly in a position to deny positively such a possibility. However, appearances in the three months' gland argue strongly against a previous invasion with lymphocytes, and, in my opinion, the almost complete absence of the lymphoid cells in the stroma at that stage, together with the presence of undoubted transitional forms between the reticular epithelium and the small cells, speaks unequivocally in favor of the epithelial genesis of the small cells.

The differential structural features between the fully developed thymus and the lymph glands will be considered after having presented our detailed study of the histological elements which compose the thymus.

IV. The Histological Elements of the Thymus—(*a.*) *The Small Thymus Cells*—The small thymus cells are composed of a round, densely-staining nucleus, 3-4μ in diameter, and very scant, granular, ragged cytoplasm which is not strongly basophilic. The cytoplasm may not be distinguishable. The intensity of the nuclear staining varies in different cells and with different methods. Sometimes one may distinguish a small nucleolus and small, peripherally-disposed chromatin granules. In the majority of cells of this type the nuclear substance takes an intense and diffuse stain so that a nucleolus or nuclear membrane cannot be made out.

The location and distribution of the small cells in the lobules varies with different glands and with the different stages of evolution and involution. In general they are found most closely aggregated in the cortical zone.

It is possible to demonstrate slight morphological differences between the small thymus cells and the true lymphocytes found in the lymph nodes, although they are so slight as to make an absolute differentiation by the usual methods oftentimes impossible. If, however, smears be made directly from the cut surface of the thymus and a lymph node on the same slide and stained by Giemsa's method after fixation in methyl alcohol, it will be seen that most of the lymphocytes show a definite, sharply circumscribed, protoplastic cell body, which takes an intense basophilic stain, and may contain azur-granules and vacuoles. The small thymus cells, on the other hand, rarely show any distinguishable cell body; where the narrow fringe of protoplasm surrounding the nucleus is visible, its margin is ragged and indefinite and the basophilic staining is never marked.

Shridde (19) has called attention to the absence of granulæ in the small thymus cells, and lays stress upon this as an important differential point.

As regards the structure and size of the nucleus, in Giemsa smear preparations, no differences could be made out between lymphocytes and small thymus cells.

Even in the fully developed gland, definite protoplasmic connections may sometimes be seen between the small round cells and the reticular cells. Hammar attributes this to the result of faulty fixation, especially the use of Zenker's or other bichloride containing fluid. He states that when Fleming's or Tellyesniczky's fluid is used as a fixing agent, such pictures are not found. I cannot agree with this statement, since I have seen transitional cell forms in preparations fixed with these reagents. Many of the small round cells do, however, lie free in the protoplasmic reticulum formed by the reticular elements, and by the use of the ordinary staining methods are indistinguishable from lymphocytes.

I have been able to demonstrate definite mitotic figures in but one of my preparations. This is due probably to the difficulty in obtaining perfectly fresh material at autopsy, and in part, also, to the small size and dense staining of the nuclear substance.

In reviewing the literature upon the histology of the thymus, I have found very little emphasis laid upon the regressive changes so frequently found in the nuclei of the small thymus cells. These changes have been so constantly found, both in normal and diseased cases, that I am inclined to attribute to them a functional significance. Briefly stated, these nuclear changes consist in a pycnosis of the nuclear substance, with budding and the extrusion of nuclear particles. The forms assumed by the nuclear body under these circumstances are varied in the extreme. Very often one sees several rounded knobs protruding from the surface, and by carefully focussing in different planes, the entire nucleus is found to be studded with knobby prominences, so that it takes on a mulberry shape. Sometimes the nuclear extrusions are pyriform in shape, being attached to the nuclear body only by a delicate stem. Dumbbell forms are also frequently met with. Whether these represent atypical mitoses, as Marcus (15) believes, or merely a fragmentation of the nucleus, I cannot say. It has not been possible to follow definitely the fate of the nuclear particles after extrusion from the cytoplasm. Free chromatin particles have been seen lying in the protoplasmic meshwork formed by the reticular cells; moreover, as I shall describe later, nuclear fragments as well as fairly well-preserved rounded nuclei, are found within the reticular cells and in the Hassall bodies.

Since this process of nuclear extrusion and disintegration is both widespread and more or less constantly found during all stages of development of the gland, and is present in freshly obtained material, after fixation by various reagents, it cannot be ascribed to post-mortem change or to technical artefact. Marcus has advanced some very interesting theories as to the significance of these nuclear changes. His studies were made on the amphibian thymus (Gymnophiona), and deal with the life-history of the thymus cell from the point of view of the cytologist. He proceeds from the observation that during the very active development of the gland cells there occurs a reduction in the mass of cytoplasm out of all proportion to the reduction in the mass of the nuclear substance. As a result of this disturbance in normal balance between nucleus and cytoplasm, the small thymus cell enters upon an inactive phase in which it is unable to perform its normal functions of assimilation and reproduction. A certain number of the cells therefore disintegrate. Others, however, through the extrusion of chromidia into the cell plasma or through atypical mitoses, succeed in ridding themselves of surplus nuclear material and restoring the normal balance between nucleus and cytoplasm. The conditions are now suitable for a further growth and differentiation of the cells, in the course of which they increase in volume and

give rise to the epithelioid and reticular elements of the gland, and even the Hassall bodies, eosinophilic cells, and myoid cells. This line of development is therefore the reverse of that assumed by Bell, Stohr, and Prenant and the writer, who believe that the small cells are developed from the large epithelial cells.

According to Marcus, then, the nuclear changes above described are an expression of the attempt on the part of the small thymus cells to prepare themselves for further differentiation and development. I wish in this connection, however, to venture the suggestion that the discharge of plasmosomes from the nucleus may also in some way be associated with the elaboration of the active secreting substance of the gland. We shall recur to this later in endeavoring to interpret our histological findings.

The small thymus cells are said by Hammar (20) to possess ameboid motion, and this attribute has been used by him as an argument in favor of their lymphocytic nature. Against his observations, there is only a single negative observation of Basch (21) upon the thymus cells of the pigeon. Hammar's studies were made on the thymus cells of frogs and turtles, using the aqueous humor of the eye as a medium. His sketches illustrating the supposed migratory powers of the lymphoid cells are, to my mind, by no means convincing. The cells which he has depicted are so irregular in shape that a change of position due to currents in the hanging drop or in the focal plane would give rise to a distinct alteration in the outline of the cells. The pseudopodia which he has sketched in outline may well represent the nuclear extrusions which I have described. This seems to me probable for the reason that the cytoplasm of the typical small round cells is so scanty that it would not suffice for the formation of large pseudopods. Finally, assuming Hammar's observations to be correct, such slight mobility as his pictures indicate is hardly an overpowering argument for the lymphocytic nature of these cells.

Another argument advanced by Hammar is based upon the sensibility of the small thymus cells to the action of the Röntgen ray. Rudberg (22) has shown that an exposure of a few hours to the X-ray is sufficient to cause an almost complete disintegration of the small thymus cells; the large reticular cells are more resistant to Röntgenization and succumb only after prolonged and repeated exposures. The small thymus cells, therefore, resemble the lymphocytes in their sensitiveness to this agency. This argument by analogy, however, is obviously not conclusive. The marked susceptibility of certain epithelial cells, notably the spermatogenic cells, is too well known to need further comment.

(*b.*) *The Reticular Cells*—Very early in development, one may distinguish from the small, densely stained round cells, larger elements, which form a considerable portion of the glandular substance. These are the so-called reticular cells, which in the course of their further development exhibit many remarkable morphological peculiarities. During the natural or abnormal involution of the gland they show a greater resistance than the small, round cells and persist after the gland has lost its lymphoid appearance. During the period of most active growth, the reticular cells are less prominent in the general picture because they are overshadowed by the very numerous small thymic cells. One may almost always, however, distinguish a marginal zone, where the small cells are less abundant, from the medullary zone where the reticular cells are relatively conspicuous; and it is only in the gland showing a most active proliferation that the reticular elements are not readily to be distinguished. Under all circumstances one may, in thin sections, identify at least the nuclei of the reticular elements from those of the small thymus cells.

So varied are the reticular cells in their shape and size that an accurate verbal description is difficult. I can only note as concisely as possible some of the most striking characteristics of these cells. The nuclei exhibit no special differential features. They are considerably larger than those of the small thymus cells; most commonly round or oval in shape; relatively poor in chromatin; the nuclear membrane distinct. A small nucleolus is usaully present. In polychrome stains the nuclei of the reticular cells take a more purplish, those of the small cells a more bluish stain. They may attain a very large size, and under special conditions undergo a peculiar hydropic degeneration.

The cell outlines are indefinite, the cell protoplasm being drawn out into irregular prolongations, which form extensive protoplasmic intercellular connections. In a general way one must conceive of the reticular cells as forming a loose syncytium—the whole constituting a protoplasmic meshwork, in the cavities of which lie the smaller elements of the thymus. While under exceptional circumstances the individual reticular cells may become discrete, this is never seen in the normal organ; and while it is manifestly impossible to trace every protoplasmic filament to its termination the intercellular connections are everywhere in evidence. The structure of the reticulum in this respect resembles that of the pineal gland.

In addition to these irregular protoplasmic cell connections the reticular elements are seen to contain distinct fibrils. These are formed upon the surface of the cell; they extend from one cell to another and run a fairly straight or slightly bent course. They are usually not branched. They are brought out most distinctly by the Mallory phosphotungstic stain, taking an intense blue color in distinction to the collagenous fibrils which are stained brick-red. The number of these fibrillæ is not great, nor do all the reticular cells undergo this fibrillary differentiation. In some cells the fibrils, running a more or less parallel course, may form a sling about the nucleus.

The cells of the reticulum exhibit marked phagocytic powers towards the small thymus cells. This occurs both in the course of normal involution, but especially under pathological conditions. The cells taken up are always of the lymphoid type; the densely staining pycnotic nucleus may however preserve its normal contour; it is usually surrounded by an unstained narrow areola. The reticular cells may be crowded with ingested small cells. Under these circumstances the reticular cells show a vacuolar degeneration and disintegrate; the nucleus is pushed to one side, becomes hydropic, loses its staining powers, and the cell finally breaks up into protoplasmic detritus.

Under certain pathological conditions associated with accidental involution of the gland, I have noted peculiar degenerative changes in the reticular cells. Similar changes have been described by Rudberg in his study of the effects of Röntgenization. The reticular cells lose their protoplasmic connections, taking on a circular or ovoid form. The cell outline becomes distinct, and one may even detect an indefinite cell membrane. The cytoplasm, which normally shows a very fine fibrillary structure, becomes vacuolated and stains very feebly with the acid dyes. The nucleus assumes an eccentric position, becomes pale and hydropic; the chromatin disappears, and the cytoplasm undergoes granular disintegration. It has seemed to me that these changes in the reticular epithelium are seen especially in the course of infections.

The relation of the reticulum of the thymus to the small thymic cells is in principle comparable to that between the neuroglia and the true nervous elements. In both instances we have a syncytial supporting structure of epithelial origin, capable of forming anastomosing fibrils through a peculiar differentiation of the cell protoplasm. Both the neuroglia cells and the reticular epithelial cells of the thymus may under pathological conditions become separated from the fibrillar meshwork, lose their cytoplasmic connections with other cells, exhibit phagocytic properties, and undergo retrogressive changes.

(*c.*) *The Hassall Bodies*—There has been much discussion as to the origin and significance of these characteristic structures. They have been variously interpreted as rests of the original excretory ducts, Schambacher (23), as rests of epithelium which have not become transformed into lymphocytes, Nussbaum and Prymak (12), as degenerate remains of the original epithelial anlage, His (2), Stieda (3), as structures derived from the connective tissue, Amman (24), Watney (20), or taking their origin from the endothelium of the blood vessels, Cornil and Ranvier (26), Afanassiew (27), Demoor (28), Nussbaum and Machowski (29). Hammar and Bell have shown all these views to be wholly or in part erroneous, and have traced the development of the Hassall bodies form hypertrophic reticular cells. The formation of these structures begins fairly early in fetal development, and continues long into the post-natal evolution of the organ. The Hassall bodies cannot therefore be considered merely as embryonic rests, but arise at any time during the period of active growth.

Wallisch (30) has proved this point, by making painstaking measurements of the total area of Hassall bodies in cross-sections of the entire thymus. His calculations indicate a progressive increase in the volume of the Hassall bodies as compared with that of the gland, both during fetal life and early childhood, so that in young children the total volume of the Hassall bodies exceeds that of the whole thymus in a three months' embryo.

I have little to add from my personal observations to the very complete description which Hammar has given. The various stages of development, from irregular cell complexes composed of large overgrown reticular epithelial cells, to the typical onion-like Hassall body, have been frequently noted. It is easy to demonstrate also the protoplasmic processes given off by the flattened peripheral layer of cells, uniting them to the reticular cells. The exquisite fibrillary structure of the cells comprising the Hassall bodies is especially well brought out by Mallory's phosphotungstic-hematoxylin stain. The fibrillæ are wavy, of different thicknesses, and may in places run a parallel course. More commonly they form a highly irregular basketwork throughout the cells. Under very high magnification some of the individual fibrillæ are seen to be studded with granules, which may be arranged at fairly regular intervals, so as to suggest

a cross-striation. This is of interest in connection with the so-called myoid cells to which we shall refer later.

The confines of the individual cells composing the Hassall bodies are never distinct, and there appears to be a true fusion of the protoplasm of adjacent cells. The resemblance of the Hassall bodies to epithelial pearls is a superficial one. Prickle cells or intercellular bridges (other than the fibrillary connection) are wanting, and though the degenerative processes affecting the inner layer of cells at first glance simulate keratinization, the presence of either keratin or keratohyalin granules cannot be demonstrated with the appropriate stain.

Necrotic changes in the Hassall bodies usually do not occur, save in post-natal life. The different steps are not easy to demonstrate, but as an end result we find large cystic spaces lined with one or several layers of flattened syncytial reticular cells; the cysts are filled with irregular flakes and masses of eosin-stained material, which may undergo partial calcification. Such cysts may attain a size of a millimeter or more, so as to be easily visible with the naked eye as white foci.

In the smaller Hassall bodies sharply defined circular spaces occur, often containing nuclear fragments or acid-staining detritus. The formation of these circumscribed cystic spaces can be readily traced. The process begins in a rarefaction of the protoplasm about the nucleus, with a disappearance of the fibrillar structure. Towards the periphery the fibrillæ become denser and tend to run concentrically. The nucleus shrinks, loses its basophilic staining property, and finally undergoes solution. The peripheral protoplasm becomes condensed and undergoes a change in its staining reaction. On a few occasions I have noted the presence of indistinct fibrillæ attached to the margin of these vacuoles, probably the frayed-out remains of the intracellular fibril meshwork. Hammar and others have described cystic spaces within the reticular cells, which are lined with distinct cilia; and speaks also of "Flimmer-krater," *i.e.*, cells whose concave free margin is clad with a row of cilia. In the human thymus I have not found free ciliated cells and think it possible that Hammar may have interpreted as cilia the attenuated intracellular fibrils, which may in places show a parallel arrangement.

Liquefaction of the protoplasm of the reticular cells with condensation of the periphery has been described by Ver Eecke (16) in the frog's thymus and considered by him as a secretory process. Bell (7), in his study of the Hassall bodies in the pig embryo, also attributes a secretory function to these structures. The peculiar transformation of the protoplasm of the component cells into "colloid"* is according to him not to be regarded as a process of degeneration, for the reason that this takes place before the onset of regressive changes in the remaining constituents of the organ. How far such an interpretation is justified, we shall consider presently.

(*d*) *Goblet and Mucous Cells*—Isolated cells filled with a homogeneous, mucin-like substance are found amongst the reticular elements in considerable numbers in the thymus of fish, reptiles, amphibians, and birds. So far as I know they have not as yet been described in the mammalian thymus. I have not infrequently found cells in the human thymus containing one or several globules of a refractile, homogeneous substance, which may distend the cell-body aand crowd the nucleus to the periphery. The globules in polychrome-stained preparations assume a uniform greenish-blue color, similar to mucin or colloid. Whether these cells are analogous to the mucous cells of the lower vertebrates, I cannot positively state, but consider it probable. I have never found true "goblet" cells with a free secreting surface.

(*e.*) *Myoid Cells*—These peculiar structures were first described in 1888 by Sigmund Mayer (31) in the frog thymus. They were long, spindle-shaped elements showing distinct cross-striation, and closely resembling atypical or rudimentary voluntary muscle fibers. By Mayer they were interpreted as such, and their presence within the thymus explained as a secondary inclusion.

Schaffer (32), in 1893, noted similar cells in the Teleost thymus, describing them as sarcolytes in various stages of disintegration.

Their presence in the thymus of birds and reptiles was discovered by Pensa (33) in 1902. He found the muscle-like cells particularly numerous and well marked in the chicken thymus. He also called attention to the presence of large oval cells with concentrically arranged striated fibrillæ. Pensa states specifically that the myoid cells are not found in man.

The origin of the myoid cells is ascribed by him to the inclusion of embryonic muscle fibers derived from the branchial or pharyngeal musculature. In serial sections

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* The term "colloid" is used by Bell in a purely descriptive sense, without reference to the chemical nature of the substance in question. For the detailed description of the mode of formation and varieties of the Hassall bodies, I would refer to the original article.

of the frog thymus he was able to demonstrate the close apposition of a bundle of muscle fibers derived from the depressor mandibulæ to the thymus lobules.

Hammar (18), in 1905, in his study upon the histology of the thymus, was the first to suggest a different origin for the myoid cells. He regarded them as peculiarly differentiated hypertrophic reticular cells, and therefore unrelated genetically to true muscle fibers. Nevertheless, by pointing out the presence of an X-striation and "Mittle-Scheibe," he demonstrated the close morphological similarity between the myoid cells and true muscle fibers. The relationship of the myoid cells to the reticular epithelium was shown by the presence of transitional forms and protoplasmic connections. In the round or oval forms the fibrillæ which ran a concentric course at the periphery of the cell showed an exquisite cross-striation.

Pensa (34), in 1905, denied Hammar's contention as to the presence of protoplasmic connections both between the reticular cells, and between the reticular and the myoid cells. In favor of the inclusion theory he quoted an analogous observation of Glas (35) upon the presence of striated fibers in the tonsil.

Weissenberg (36), in his careful study of the myoid cells in birds, comes to essentially the same conclusions as Pensa. He regards the myoid elements as atypical muscle fibers, included within the thymus, while still in an undifferentiated state, and later developing their characteristic striation. He was, however, unable to trace the ingrowth of muscle fibers into the thymus.

Dustin (37), in a recent study of the myoid cells of the frog's thymus, has propounded still another theory as to their origin and significance. The thymus in the frog, as Ver Eecke has shown, undergoes marked seasonal variations in structure. During the period of active functioning, *i.e.*, in the summer, there is a renewed vascularization of the thymic lobules, the new-formed capillaries arising from endothelial sprouts in the usual manner. Later, the capillaries undergo involutional changes, and at the same time the spindle-shaped structures in the connective tissue sheath take on a fibrillary differentiation, and develop into full-fledged myoid cells. They are therefore in some way concerned in the involution of the blood vessels. In the winter frog, the myoid cells themselves, undergo degeneration and are relatively less numerous. Dustin accordingly rejects Hammar's view as to their epithelial nature, and is in disagreement also with the "inclusion" theory of Pensa and Weissenberg. His own theory, however, would seem to apply only to those cold-blooded animals in which the thymus is subject to seasonal variation.

So far as I have been able to find in a careful review of the literature, myoid cells have never heretofore been described as occurring in the mammalian thymus. In sections of a five and one-half months' human embryo thymus, fixed in Zenker's fluid and stained with Mallory's phosphotungstic hematoxylin, I was so fortunate as to find very numerous, typical myoid cells, identical in all respects with those described in the thymus of fish, amphibians, reptiles, and birds. The cells are long, spindle-shaped or irregular band-like structures, most numerous in the cortical portions of the lobules. They occur singly or in groups, the individual fibers running a more or less parallel course. Under high magnification, one may readily distinguish a longitudinal fibrillar structure and a transverse deeply stained striation of varying width. Occasionally, only some of the fibrillæ in a cell exhibit alternating light and dark spaces, the remaining fibrils staining diffusely. The large oval nuclei are surrounded by an undifferentiated protoplasmic zone; they are situated for the most part on the surface of the cells, less frequently within the substance of the fiber.

With the staining methods employed I was not able to detect any intermedial transverse line in the unstained zone, nor the lighter "Mittel-Scheibe" within the stained portion of the discs. Since these structures have been clearly described and pictured by Weissenberg, Pensa, and Hammar, it is probable that appropriate methods would likewise demonstrate their presence in the human thymus.

As regards the significance of these cells, I am in accord with Hammar, and in disagreement with Mayer, Schaffer, Pensa and Weissenberg and Dustin. I have not only seen undoubted protoplasmic connections between the myoid cells and the reticular elements, but I have also on one occasion found distinct cross-striations in the crescentic peripheral cells of a Hassall body. These facts seem convincingly in favor of the close genetic relationship between the myoid and the reticular elements. In the thymus of a new-born child I have also found indistinct cross-striations in some of the individual fibrils of the reticular epithelium.

Since the embryonic material at my disposal has been very limited, it is not possible to say as yet whether the myoid cells occur regularly in the fetal thymus or whether their presence is exceptional. It is certain that they are not regularly present in post-natal life. Weissenberg has shown that the myoid cells in chickens

undergo regressive changes, and are entirely wanting in advanced age. It is probable, therefore, that in the mammalia such regressive processes also occur at an early age.

In this connection, I wish to refer to the occurrence of the myoid cells in the pineal gland. These have been described by Dimitrowa (38), Nicholas (39), and Studnicka (40) in the pineal gland of the ox, but have not been seen in other vertebrates. I have found similar cells in a mixed tumor of the pineal gland in man. In appearance they are identical with the myoid cells of the thymus. There is the same obscurity as to their origin and significance as in the case of the striated thymus cells.

(*f.*) *Epithelial Ducts Cysts and Solid Inclusions*—Under this heading we may consider briefly certain epithelial structures found occasionally within the gland either during fetal life or after birth, which differ from the remaining parenchyma in their appearance.

They may take the form of solid, sharply circumscribed nests of cells, of cystic spaces lined with low cuboidal epithelium, or of blind ducts ending in solid, irregular cell strands. Pepere (41) has recently made the attempt to interpret these various types of epithelial rests as one accessory parathyroid system. It seems to me that this is rather arbitrary, as most of these structures bear not the slightest resemblance to normal parathyroid tissue.

Schambacher (23), Sultan (42), and Simmonds (43), amongst others, have described blind ducts found principally in the interlobular septa. In nine-centimeter (three or four months) human fetus I noted in the interstitium between the lobules numerous branching ducts lined with a single layer of low cuboidal epithelium, the nuclei of which are identical in size and appearance with those of the reticular epithelium. When traced through serial sections, the ducts are found to coalesce with one another, and to end blindly in solid epithelial cell nests. The lining epithelium is not ciliated, but in places there is a fairly distinct cuticular membrane on the inner surface. There is no sharply defined basement membrane. I have found similar ducts in isolated sections of the child's thymus, lying principally within the interlobular stroma, but occasionally found also in the peripheral portion of the lobules. Large irregular cystic spaces lined with a single layer of low cuboidal epithelium were found on one occasion in a seventeen-year-old thymus.

Schambacher has advanced the view that the solid prolongations of the ducts penetrating the lobules, and assuming a concentric arrangement, undergo central hyaline degeneration, and thus give rise to the Hassall bodies, and furthermore that all Hassall bodies are originally formed in this way. That the solid prolongations of the ducts are often intimately connected with the reticular cells, and may occasionally take on the characteristic differentiation of the Hassall bodies, is true; that this is the usual manner in which the Hassall bodies arise is obviously not correct. Whereas the true epithelial ducts occur chiefly in fetal life or in early childhood, the differentiation of the reticular elements into Hassall bodies, as has been already indicated, proceeds up to the time of puberty, *i.e,* the age of beginning involution. Furthermore, the epithelial ducts are not regularly found even in the fetal thymus, are never numerous, and occur principally in the interlobular septa and cortex; whereas the formation of Hassall bodies takes place primarily in the medullary portions of the lobules.

As to the origin of these dutcs it is probable that they are derived from a partial persistence of the original evagination of the third branchial cleft. In rabbits, according to Stieda (3), the thymus develops regularly as a hollow outgrowth of entodermal epithelium which later develops into solid alveoli, whereas in pigs and human beings the original anlage is solid from the beginning, but may be partially canalized. I have observed duct-like formations and distinct lumina in serial sections of an eleven-millimeter rabbit fetus. They were situated principally in the upper portion of the gland. Therefore it is very likely that the partial persistence of the original lumen may occasionally occur in the human thymus and give rise to the described cysts and ducts.

Structures, which I have interpreted as undoubted parathyroid inclusions, have been found twice; once in a one-hundred-and-ten-gram glandular thymus occurring in a male of 40 (?) years, with adhesive pericarditis and pleurisy, who showed in addition to the remarkable hyperplasia of the thymus a general tuberculous hyperplasia of the lymph nodes.* The second thymus showing parathyroid inclusions was found in a male thirty-nine years of age, dying of syphilitic cirrhosis of the liver, and showing other tertiary luetic lesions. In this case the sections showed an involution thymus, consisting principally of fat, with strands and small islands of thymic tissue. The blood vessels, especially the arteries, were thickened and the seat of

* For the use of this case I am greatly indebted to Drs. Elser and Symmers, of the New York Hospital.

hyaline changes in the media. The thymic rests consisted of small round and polyhedral cells with fibrillary processes forming a loose meshwork. The reticular cells, especially at the margins of the lobules, frequently showed a distinct epithelial character. A few Hassall bodies found were neither necrotic nor calcareous.

Within the nests of thymic tissue there were a number of circumscribed islands of epithelial cells having a totally distinct character from the surrounding thymic tissue. The cuboidal cells were arranged in irregular solid cords, one or two cells deep, lying on a distinct basement membrane. Their protoplasm was strongly eosinophilic, slightly granular, and showed no fibrillary differentiation. The cell outlines were somewhat obscure. The nuclei were oval, contained a few distributed chromatin granules, and were arranged with their long axes paralled. In places the cells were grouped about a small central lumen; there was, however, no cuticular membrane, nor were the cells ciliated. Between the cords of cells there was a loose fibrillar connective tissue containing thin-walled capillaries.

There was no differentiation of these epithelial cells into "principal" and oxyphilic cells. In all other respects these islands suggested aberrant parathyroid loblues. Since the inferior parathyroids arise from the third branchial cleft near the origin of the thymus, the opportunity for the inclusion of small accessory parathyroid lobules within the thymic tissue during development is readily afforded. As Pepere (41) has pointed out, the presence of these accessory lobules within the thymus may explain some of the tetany-like symptoms occasionally noted after complete thymectomy (44), and may also explain the occasional absence of tetany following extirpation of the parathyroid glands. It seems to me, nevertheless, that Pepere has exaggerated both the frequency and the extent of these parathyroid rests within the thymus. The marginal zone of the thymus lobules, as has been described, normally consists of one or more layers of epithelioid reticular cells, arranged with their long axes perpendicular to the margin of the lobules. With the partial disappearance of the small thymus cells during involution, the marginal layer becomes especially distinct. In tangential sections through the periphery of such lobules, the appearance will be that of a solid, sharply circumscribed nest of large epithelioid cells. Such nests are of frequent occurrence, and may well have given rise to an erroneous interpretation. At any rate, I am unable to confirm the statement of Pepere as to the habitual occurrence of an accessory parathyroid system within the human thymus.

(*g.*) *The Interstitium*—In the early human fetus (three months) the thymus lobules are separated from one another by a fairly abundant stroma, consisting of loose cellular connective tissue in which the formation of collagen fibrils is just beginning. The connective tissue cells show no special features, but tend to lie with their long axes parallel to the surface of the lobules. One may find in the stroma occasional large oval "wandering cells," such as are present throughout the fetal mesenchymal tissue. I would again emphasize the absence of lymphoid cells, either singly or in groups. The very thin blood vessels contain only red blood cells with occasional normoblasts.

The development of the stroma during later fetal life does not keep pace with the rapid proliferation of the parenchymal cells of the thymus. The individual lobules therefore become closely apposed, being separated only by thin fibrous tissue septa carrying the larger blood vessels. This condition persists until later childhood, when the connective tissue between the lobules gradually increases in amount; in addition there takes place a development of adipose tissue, beginning about the adventitia of the larger blood vessels. I have made no especial study of the distribution of fat in the normal thymus. Herxheimer (45), using Sudan III. stain, has investigated the thymus in forty-seven cases with particular reference to this point. He found fat present in the form of evenly distributed globules, in practically all cases partly within the "lymphocytes," partly free, usually most abundant in the cortex. Fat globules were present also within the connective tissue cells of the septa and in the adventitia of the capillaries and smaller blood vessels. Herxheimer concludes that the presence of fat globules within the thymus cells does not indicate a degenerative process, since it is regularly found, has a characteristic distribution, and occurs in otherwise normal glands.

In previous articles, Kaiserling and Orgler (46), and Orgler (47), found that these globules were largely double refractive substances related to the myelins.

With the increase in the relative space occupied by the stroma, the connective tissue also becomes denser and more fibrous, and in later life tends to undergo hyaline transformation.

It is to be noted that the septa between the sharply circumscribed lobules do not normally penetrate the gland, save for a thin sheath accompanying the blood vessels, In fetal life and in early childhood, the adventitia of the blood vessels is represented,

in Mallory aniline-blue preparations, by a single blue-stained line. Later, the adventitia of the intralobular arteries and veins becomes more abundant, and connective tissue fibrils may penetrate the glandular substance for a certain distance about the larger vessels. In the normal gland, however, even in well-advanced involution, the lobules are remarkably free from connective tissue. The true reticulum, as I have already stated, and as has been thoroughly shown by Hammar and Prenant, is formed by the interlacing protoplasmic processes of the larger epithelial cells of the gland.

Under patholigical conditions, the relation of the stroma to the lobules deviates at times from that above described, and there may occur a true sclerosis of the thymus, To this we shall refer later.

(*h.*) *The Oxyphilic Cells*—The presence of mononuclear cells with distinct large eosinophilic granulations was first noted by Schaffer (32) in 1893, since which time they have been regularly recorded by all writers upon the histology of the thymus. They are found in greatest abundance in the interlobular septa in the neighborhood of the blood vessels, and especially in those regions where the reticulum abuts directly upon the stroma, without the intervention of the cortical portion, but they are present also in considerable numbers in the cortical portion of the lobule.

In sections of a three months' human embryo they were present, though scarce. This controverts Stohr's statement that they first appear in the fifth month of fetal life. They are found throughout the entire period of evolution, but are especially numerous during the first years of childhood. In the involuted thymus, I have usually found them wanting.

What is the significance of these cells? Most writers who have given them their attention have interpreted them as eosinophilic leucocytes arising in the perivascular tissues and migrating into the gland substance, and largely because of this finding have ascribed to the thymus a hematopoietic function during fetal life. Morphologically, however, these cells do not resemble either the polymorphonuclear eosinophiles or the cosinophilic myelocytes. The cells are ovoid or elliptical in shape, and in size they are slightly larger than the ordinary plasma cell. The relatively small, spherical, deeply stained nucleus is situated at one pole near the surface, this feature serving to differentiate them from the blood elements containing eosinophilic granules.

A clue to the origin of these cells was afforded by the study of sections from an early rabbit embryo. Certain of the reticular cells in this preparation showed a very fine but perfectly definite eosinophilic granulation. No eosinophilic cells were found in the stroma. Similar reticular cells with oxyphilic granules have been noted by Hammar in the Teleost thymus. Since then, I have repeatedly noted the presence of certain cells which in my opinion must be regarded as transitional between the usual type of reticular epithelium and the ovoid eosinophilic cells above described. Scattered amongst the small and large thymus cells, one regularly finds certain large ovoid cells with eccentric nuclei, and coarsely granular strongly eosinophilic cytoplasm. These cells differ from the reticular epithelium in having a well-defined cell contour, without protoplasmic prolongations, and in the strong affinity of the cytoplasm for the acid dye; they differ also from the cells first described in not possessing discrete granulæ. They are found not only within the lobules but also in the septa, and, like the well-differentiated eosinophilic granular cells, tend to group themselves in the neighborhood of the larger blood vessels. In some thymuses they figure conspicuously in the general picture. True eosinophilic polymorphonuclear leucocytes are occasionally present in the stroma.

I would tentatively suggest, therefore, that these eosinophilic cells represent different stages of a specially differentiated form of thymic epithelium; and, since they are structurally distinct from the remaining parenchymal cells, the possibility has occurred to me that they may subserve a special function, and that the eosinophilic granulæ may represent a stage in the secretory activity of the cells analogously to the interpretation placed upon similar appearances in the hypophysis and the parathyroid. For convenience, I would suggest the term "oxyphilic" cells for these elements.

Mast-Zellen and plasma cells are at times quite numerous in the connective tissue of the thymus. I have seen them at various ages, but never in the fetal organ. They may be entirely wanting. They probably occur in association with chronic inflammatory conditions.

From the foregoing description it will be seen that the thymus differs materially in its structure from the lymph nodes and lymph adenoid tissue. It seems advisable, by way of summary, to enumerate again the important differential features.

(1.) The thymus has no definite capsule nor peripheral lymph sinus containing lymphocytes.

(2.) There is no fibrous reticulum such as is common to all lymphadenoid tissue. The reticulum of the thymus is formed by the anastomosing protoplasmic processes given off by the reticular epithelial cells. Normally, no connective tissue fibrils can be demonstrated within the lobules, save those accompanying the blood vessels.

(3.) Slight morphological differences may be demonstrated between the small thymus cells and the true lymphocytes. The cytoplasm of the small thymus cells is never sharply circumscribed, and frequently shows cellular connections with the reticular epithelium. It is never intensely basophilic and, according to Schridde, contains no Altmann granulæ.

(4.) There are no germinal follicles in the cortex.

(5.) The thymus contains peculiarly differentiated structural elements such as are never found in the lymph glands. These are

(*a*) the mononuclear oxyphilic granular cells.

(*b*) the Hassall bodies,

(*c*) the myoid cells.

These are, in shortest abstract, the arguments against the lymphatic nature of the thymus. We, therefore, in accordance with the intrinsic and extrinsic evidence, have attributed to the thymus an internal secretion. But structurally, the thymus presents little resemblance to the other ductless glands, save the still debatable epiphysis cerebri, with which it has certain histological features in common. If, then, it be true that the thymus is an organ of internal secretion, what are the active secreting elements, and how is the secreted substance elaborated? This question, so far as I know, has never been opened, nor can it be answered definitely as yet. The reticular epithelial cells and their differentiated forms, the Hassall bodies, do not suggest secreting elements. If one may interpret their striking structural characters from the point of view of functional activity, one is inclined to regard their power of phagocytizing the small thymic cells as an attempt to get rid of useless or noxious material. Their other striking features, that of producing fibrillæ, and undergoing a fibrillary protoplasmic differentiation, seem to signify a supporting function for the smaller cellular elements. There seems little reason for ascribing to the Hassall bodies a specific secretory function, as has been done by Ver Eecke and Bell. As we have shown, the Hassall bodies represent peculiarly differentiated cell-complexes of reticular epithelium, which tend to undergo regressive changes. Their concentric arrangement is in all probability due merely to mechanical causes, such as the uniform pressure of the rapidly-growing adjacent small thymic cells, from without, and the continued accumulation of cast-off, necrotic material from within. They are least numerous and of smallest size during the period when the thymus is growing most rapidly and is, presumably, most active functionally. The central portion of the fully developed Hassall body consists of necrotic and, in all likelihood, inert detritus; the peripheral cells differ structurally only in their flattened form from the remaining reticular cells.

Having eliminated the reticular epithelium and the Hassall bodies as secreting elements, there remains only the small thymus cells. We have already ventured the suggestion that the extrusion of nuclear particles into the cytoplasm might be interpreted as indicative of a secretory or ferment-producing process on the part of the small cells. How far this theory is consistent with the views of Marcus on this point, and the general laws of cytology, the cytologist must decide, nor does a full discussion of the role played by the nucleus in the specific activity of secreting cells fall within the province of this article. The subject has been taken up in considerable detail by Adami (48) in his text-book, and numerous illustrations of the discharge of nuclear particles into the adjacent cytoplasm are given. In Adami's own words "what appears to be the specific activities of particular forms of cells and particular species would seem very largely to occur through the intervention of the nucleus, through substances elaborated by and discharged from the nucleus, and this is especially true in connection with the specific secretory activities and * * * the oxidative processes." This discharge of nuclear particles associated with the normal secretory activity of the cell passes insensibly over into the pathological conditions of karyolysis and karyorrhexis. These are general questions of cellular pathology, but their application to the specific changes manifested by the small thymus cells in health and disease is interesting and suggestive.

V. The Normal Involution of the Thymus—The material at my disposal, consisting largely of thymuses from cases of status lymphaticus, would hardly seem to furnish fair data for a study of the normal evolution and involution of this organ. We are accustomed to regard a persistence of the thymus beyond the early years of childhood as essentially abnormal and characteristic especially of the lymphatic constitution. This assumption, in spite of its almost universal acceptance, requires

proof. Two questions especially need solution, before we can obtain a clear idea of the life history of the gland. At what age does the thymus reach its maximum development; what is the influence of the lymphatic constitution upon the normal involution of the thymus?

Friedleben (49) was the first to compile careful statistics of the weight of the thymus at different ages. His tabulated results, based upon cases of sudden death, are as follows:

	Average Weight.		No. of Cases.
New born	13.98....	{ 25.8 { 6.08	72
1–9 months	20.14....	{ 34.10 { 9.74	13
9 months–2 years	26.6.....	{ 37.7 { 19.97	7
3–14 years	26.31....	{ 31.9 { 19.7	6
15–25 years	21.54....	{ 23.6 { 17.8	4
26–35 years	3.02....	{ 4.21 { 1.82	2
36–74 years	13.07....	{ 28.8 { 6.0	?

According to this table the weight of the thymus increases up to the second year, then remains stationary up to the time of puberty; diminishes gradually up to the twenty-fifth year, then abruptly, to rise again in later life. Two sources of error serve to make these figures of doubtful value. The number of cases in older children and adults is small, so that the natural wide variation in the individual cases is not corrected; secondly, and of more importance still, cases associated with status lymphaticus are probably included in the statistics. The effect of disease, both acute and chronic, in reducing the weight of the thymus was known to Friedleben. The following table illustrates this influence:

Age.	Average Weight.				No. of Cases.
	Acute.		Chronic.		
Infancy	7.34....	{ 18.5 { 1.3	2.37....	{ 9.1 { 0.27	87
Childhood	10.71....	{ 20.7 { 3.7	4.56....	{ 18.75 { 0.54	45
Youth	9.70....	{ 31.9 { 1.4	4.08....	{ 8.4 { 0.9	51
Adolescence	7.55....	{ 10.2 { 5.5	5.51....	{ 7.38 { 2.68	8

From these data he concludes that in acute illness the absolute weight of the thymus is reduced to about one-third of the normal; in chronic wasting disease, to one-eighth or ninth in infancy, one-sixth in childhood, one-fourth in adolescence. The great majority of writers who have failed to take this into consideration and have based their statistics upon pathological material obtained at autopsy, give figures very much lower than those of Friedleben. Thus Boyd (50), in a large series of cases dying in the St. Marylebone Infirmary, found average weights between 3.69 and 8.51 grams during the first seven years of life. So, too, Bovaird and Nicoll (51) found the average weight in four hundred and ninety-five cases between birth and the fifth year of life to be only 5.9 grams, or less than one-fourth of that given by Friedleben for the corresponding age. This discrepancy is readily explained when we take into consideration the very large proportion of poorly nourished and marantic children, dying in the majority of cases of broncho-pneumonia and intestinal conditions, comprised in their statistics. Bovaird and Nicoll were aware of the deleterious effects of exhausting diseases upon the thymus, and quote, too, Friedleben's observations; nevertheless they draw from their tables the strange conclusion that the weight of the thymus gland as commonly given is excessive, owing to the acceptance of pathological glands as the standard for normal conditions.

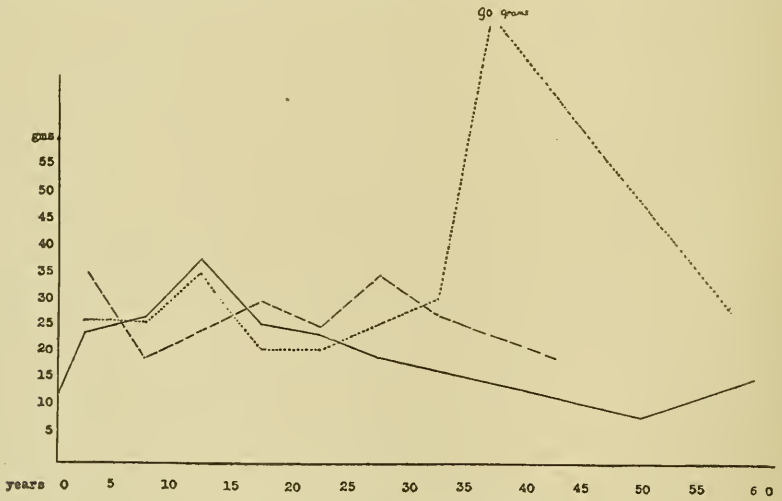
It will be seen from Friedleben's data that there occurs no decrease in the weight of the thymus during childhood and adolescence. Very few of the authors who have occupied themselves with this subject agree with this view. Amongst the few exceptions are Zoia (52), and Monguidi (53), who believed that there was a

second augmentation of growth during puberty, and Stokes, Ruhrah and Rohrer (54), who state that the thymus attains its maximum weight (twenty-two grams average) at the age of puberty, and then undergoes a gradual and progressive involution.

The only author who has given comprehensive statistics based solely upon selected cases dying suddenly while in good health from causes such as trauma or poisoning is Hammar (55). Von Sury (55a) also gives statistics based upon seventy-one cases of sudden death in previously healthy children. His figures show increase in weignt of thymus up to the ninth month, after which weight remains stationary until puberty. Only nine cases over 2 years of age are included in his statistics. His statistics are based upon eighty personally selected cases plus forty-six cases from the literature. His average weights are as follows:

New born	23 cases.	Average 13.26....	25.88 7.6
1– 5 years	23 cases.	Average 22.98....	49.0 8.5
6–10 years	5 cases.	Average 26.1.....	30.0 20.0
11–15 years	4 cases.	Average 37.52....	52.0 20.0
16–20 years	10 cases.	Average 25.5.....	47.0 15.2
21–25 years	15 cases.	Average 24.73....	45.0 7.3
26–35 years	15 cases.	Average 19.8.....	30.0 4.29
36–45 years	12 cases.	Average 16.27....	28.0 8.2
46–55 years	7 cases.	Average 12.85....	21.0 2.5
56–65 years	6 cases.	Average 16.08....	30.0 5.6
66–75 years	4 cases.	Average 6.0.....	8.0 3.0

If, therefore, we take the weight of the entire gland as a guide, we are forced to conclude that development proceeds gradually to reach its maximum at the fifteenth year, *i. e.*, the completion of puberty; during the next five years the weight diminishes



Weight of Thymus at Different Ages.

Hammar ——— Cases of sudden death from Trauma and Poisoning.
Norris ..... Cases of Status Lymphaticus.
Norris – – – – Cases of Status Lymphaticus dying suddenly from Trauma or Poisoning.

rapidly, and from the twentieth year gradually, to rise again in the last decade of life. One cannot, however, accept this conclusion outright, since the total weight of the organ is not an accurate index to the amount of functionating tissue present, and

a microscopic examination is therefore necessary by way of control. Hammar has endeavored to supply the gap and to fortify his conclusion by the use of the following ingenious method: Thick cross-sections through the entire gland were traced under low magnification and the boundaries of interstitial tissue and parenchyma plotted out. The tracings were then transferred to wax plates of uniform thickness, and the component parts, *i. e.,* stroma and parenchyma, cut out and weighed separately. By means of a simple formula based upon the specific gravity of the thymic parenchyma, the fat and connective tissue, an approximate computation could be made, showing the absolute weight of thymic parenchyma in each case. The curve plotted from the data obtained in this way corresponds pretty accurately to the curve of total weight. The maximum is again reached at the age of fifteen, and from this point declines abruptly.

If it be granted, then, that the functional activity of the gland is correlated with the amount of thymic parenchyma present, the conclusion seems inevitable that the thymus is in an evolutional state until the time of adolescence, and that involution begins at this period rather than in early childhood. In establishing this fact Hammar has cleared the ground for all serious study of the effects of pathological conditions upon the thymus.

One objection only may be raised against Hammar's figures. He may have included in his series a certain number of cases of Status lymphaticus. No mention is made by him of this condition, and it is reasonably certain that he made no attempt to exclude these cases from his observations. The statistics which Dr. Norris has compiled from cases studied at Bellevue Hospital are of service in estimating the influence of the lymphatic constitution upon the weight of the thymus at different ages. His figures differ from those of Hammar in that they are based upon pathological as well as normal cases, all of which, however, exhibited more or less pronounced evidence of the status lymphaticus. This condition was encountered in fifty-three out of approximately two thousand autopsies or, roughly, two and one-half per cent. of all cases.

Our statistics, tabulated in conformity with those of Friedleben and Hammar, are as follows:

0– 5 years	9 cases.	Average weight 27.7
5–10 years	4 cases.	Average weight 26.0
11–15 years	3 cases.	Average weight 35.0
16–20 years	12 cases.	Average weight 21.4
21–25 years	12 cases.	Average weight 21.1
26–30 years	6 cases.	Average weight 25.4
30–35 years	4 cases.	Average weight 28.2
35–40 years	2 cases.	Average weight 90.0
55–60 years	1 case.	Average weight 27.5

A comparison of these figures with those of Hammar is best shown in the preceding chart.

It will be noted that the two curves are almost identical up to the twentieth year; beyond this, the curve of weights diverges, Hammar's falling and ours showing a distinct rise. The excessive rise to ninety grams during the fourth decade must be regarded as distinctly abnormal, since the two cases upon which the average was based—one a case of general tuberculous lymph adenitis and adhesive pleurisy, with a one-hundred-and-ten-gram hyperplastic thymus, the other a case of acromegaly with a seventy-gram thymus—were highly exceptional instances of true thymic hyperplasia in late life. So also the twenty-seven-gram thymus during the sixth decade, occurring in association with exophthalmic goiter, does not represent a true average weight.

Although our statistics are based upon a relatively small number of cases, a clear inference may be drawn as to the effect of the lymphatic state upon the weight of the thymus. Our curve practically corresponds with that of Hammar, during the pre-adolescent period, although our cases included pathological conditions which would tend to reduce the thymic weight; whereas Hammar included only normal and, possibly, many status cases. The logical inference is that the average weight of the thymus, when associated with Status lymphaticus, is in excess of the normal average, since the adverse effect of various pathological conditions is neutralized.

The marked ascent in our weight curve during the post-adolescent decade needs further discussion. Here the proportion of cases of sudden death from violence or intoxication is very large, and the influence of the associated status more patent than in the earlier years. It is the writer's personal view that this rise in weight is due to a failure of the thymus in these cases to undergo involution at the customary age of puberty. We obtain support for this view from a study of a curve of average

weights based solely upon cases of Status lymphaticus which died suddenly from violence or poisoning. Through the courtesy of Dr. Schultze, coroner's physician, we have been able to obtain data on twenty-eight cases of this sort. Our figures are as follows:

0– 5 years	7 cases.	Average weight 36.2
6–10 years	1 case.	Average weight 18.0
11–15 years	0 case.	Average weight ....
16–20 years	5 cases.	Average weight 30.0
21–25 years	8 cases.	Average weight 26.9
26–30 years	4 cases.	Average weight 35.2
31–35 years	3 cases.	Average weight 19.5

The maximum weight is attained in the third decade instead of in the second, as in Hammar's chart. The excessive weight of the thymus during the first five years is due to the inclusion of two abnormally large thymuses each weighing sixty grams. Although the data are not numerous, they indicate clearly enough the influence of the lymphatic constitution in retarding the involution of the thymus. This view is further borne out by the microscopic findings in these cases. The picture presented corresponds in a general way to that of the preceding decade.

As a result of the foregoing analysis we are in a position to answer the two fundamental questions as to the age of maximum development and the influence of the lymphatic constitution upon the normal evolution of the gland. We have found that the thymus grows steadily throughout childhood up to the period of puberty, reaching the height of its development at or about the fifteenth year. Both parenchyma and stroma share in this growth. From the time of puberty onward, the gland normally undergoes involutional changes, at first rapidly, later more slowly. Since there is present even in senescence a certain amount of thymic parenchyma, we have a right to assume that even in adult life the thymus plays a part in the economy of the body.

The influence of the lymphatic constitution is manifested in a retardation of the normal involutional changes, so that the maximum development is attained not as normally, at the time of puberty, but in the third decade. During childhood we must not expect, therefore, to find distinctive structural features in the thymus of Status lymphaticus cases, although we have seen that the weight of the gland in these cases is probably somewhat in excess of the normal average.

We are now ready to consider the involutional process somewhat more in detail and from the histological viewpoint. In sketching out in a general way the manner in which the thymus changes from a glandular organ to a mass of fat or fibrous tissue, I shall follow closely the excellent description of Hammar; my own studies are confirmatory of his in all essentials. Hammar has also pointed out the effects of various pathological conditions and nutritional distinctions in bringing about what he terms an "accidental involution" of the thymus, and has given criteria for differentiating the normal regressive changes from the accidental changes due to disease. As a matter of fact, the lines are rarely sharply drawn, and it is frequently difficult to separate the changes due merely to advancing age and those due to previous illness. This would seem almost self-evident, since few persons reach adult life without at some time having suffered disease.

The essential features of involution are plainly a gradual disappearance of the parenchymal epithelium and a replacement with fat and connective tissue. Hammar has shown, and I am fully in accord with his view, that, normally, there is no marked invasion of the lobules with connective tissue, so that the natural involution is in no sense a sclerosis of the gland. I have found this to hold true even at an age when a few irregular strands and islands of reticular cells are the sole remnants of the original gland. Aside from the thickened adventitia of the blood vessels, the circumscribed rests of thymic tissue are virtually free from connective tissue. In the secondary atrophy, due to wasting disease, the conditions, as we shall see, are different.

The histological appearance of the thymus at various ages may now be briefly delineated; the essential features are clearly illustrated by the plates appended to Hammar article.

In the earliest period (up to ten years) the parenchyma is abundant; the differentiation between cortex and medulla is not sharply defined, because of the predominance of the small cells throughout the lobules. The reticular cells are therefore not much in evidence. The lobules are closely apposed, being separated only by thin fibrous septa. The intra-lobular blood vessels have no well-developed adventitia.

During the period of childhood and puberty the differentiation into cortex and medulla becomes more pronounced. Growth centres are present in the cortex, which may have a follicular structure. The interlobular septa are broader, the vessels are beginning to develop an adventitia.

During adolescence and early adult life there is already noted a diminution in the amount of parenchymal substance. The differentiation into cortex and medulla is still present, but the follicular structure of the cortical zone tends to disappear. The stroma is relatively abundant, the septa broader; there is a variable amount of adipose tissue developed about the larger blood vessels. The vessels themselves show an increase in the muscular coat, and particularly in the adventitia. From this time on there is a progressive reduction in the amount of parenchymal tissue; the lobules become reduced in size and irregular in shape. The differentiation into cortical and medullary portions becomes obscured. The reticular cells become the predominating elements, and the marginal zone, through the partial disappareance of the small cortical cells, is frequently very distinct and prominent. The Hassall bodies undergo regressive changes but, owing to the rarefaction of the intervening parenchyma, may appear to be relatively numerous. The interstitial tissue occupies a relatively large amount of the original volume of the thymus. The fibrous tissue tends to undergo hyaline degeneration, and very few cellular elements are present in the interstitium. The oxyphilic cells disappear. The amount of fat present in the stroma varies greatly in different cases, and seems to bear some relation to the general adiposity of the individual.

In senescence, as is well known, thin strands of thymic tissue, consisting principally of reticular elements, are regularly to be found. We owe to Waldeyer (56) a recognition of the fact that the thymic fat contains presumably functionating elements throughout life. Hassall bodies are still to be seen, but appear to be diminished in numbers, so that some of them are undoubtedly resorbed. The statement of Lortat, Jacob and Thaon (57), however, that Hassall bodies are never found in the involuted thymus, is erroneous.

The precise cellular changes which take place in the thymus cells, leading to a reduction in the parenchymal substance in adult life, have not been followed, nor am I in a position to give a final answer to the problem. Nevertheless, certain structural changes, which I would interpret as regressive in their nature, have been repeatedly noted in the normal thymus of persons dying suddenly. These have already been described in part. The small thymus cells throughout life are constantly becoming pycnotic; their nuclei fragment, and they undergo dissolution. A phagocytosis of the pycnotic nuclei and of the nuclear fragments by the reticular epithelium may be seen in normal glands, although the phagocytosis is never so extensive as under pathological conditions. In the process of taking up the small cells of certain of the reticular elements disintegrate. Since the building up of Hassall bodies at the expense of the epithelial cell complexes takes place throughout the formative period of the organ, and since these structures are constantly undergoing regressive and necrobiotic changes, the loss of another portion of the reticular elements is accounted for. These I believe to be the main features in the reduction of the glandular substance.

The changes in the stroma have already been described in sufficient detail. The relative increase in the stroma and interstitial fat is to be considered as a replacement growth. Hammar has clearly shown by the wax plate method that this increase is only relative, and that the total volume of the interstitial tissue diminishes with the involutional changes in the parenchyma.

VI. The Pathological Histology of the Thymus—*Introduction*—The pathological histology of the thymus has been comparatively neglected. So far as the writer has been able to discover, no detailed study of the histological lesions has been made upon an extended series of cases. Hammar's article is concerned less with the finer histological details than with the coarser changes in the weight and structure of the gland associated with disease in general. The isolated reports found in the older literature are for the most part based upon erroneous conceptions of the normal structure. In view of these facts, it is our intention to present in detail our study of the thymus: *a,* in cases of Status lymphaticus; *b,* diseases of the ductless glands; *c,* congenital syphilis, and *d,* acute and chronic infections and wasting diseases. As we have had no personal material, we shall not attempt to consider the interesting subject of thymic tumors.

(*a.*) *Status lymphaticus*—It might have been expected that the cases of sudden death without known cause in subjects showing the thymico-lymphatic constitution would prove especially instructive. It has been commonly assumed that the thymus is in some way concerned in the mysterious death of some of these individuals, although as we have shown conclusively the mere "persistence" of the gland in

adult life is neither abnormal nor an essential feature of the lymphatic constitution.

The histological examination of the thymus in these "idiopathic status" cases was disappointing, and yielded no facts which would justify positive conclusions. Although no characteristic changes were discovered, it seems worth while to give a detailed report of the findings in these cases, since my material has been unusually abundant and amply suffices to establish the absence of characteristic lesions.

Case I.—Male; Hungarian; 21 years of age; stableman. History of privation for past two months. Found dead one evening a few minutes after having been seen in good health and spirits.

Necropsy, performed fifteen hours after death, revealed no cause of death save the anatomical features of Status lymphaticus. Both external and internal signs were marked. The thymus in this case weighed 19.5 grams, was fleshy in appearance, with visible Hassall bodies.

Microscopically, there was found a moderate amount of parenchymal substance; the somewhat irregular lobules were well circumscribed, but separated from one another by wide septa of loose fibrillary connective tissue and fat. The differentiation of the individual lobules into cortex and medullary portions was in many places indistinct. The marginal zone, composed of several layers of large epithelial cells, was very conspicuous. The cortex showed fewer small cells than usual at this age, and there was no follicular structure. The bulk of the parenchyma was formed by the large reticular cells.

Under high magnification the small cells exhibit very marked pycnosis and fragmentation of the nuclei. In many fields no normal cells of the small type are found. In the meshes of the reticulum are seen numerous small nuclear fragments, staining imperfectly with the nuclear stains. The reticular epithelial cells are, in general, well preserved, and do not show the vacuolar degeneration frequently seen in infectious processes. Phagocytosis of the small cells by the reticular elements was not observed in spite of careful search. The stroma showed nothing of interest. Very few of the typical ovoid cells with oxyphilic granulæ were found, and no mast cells. The Hassall bodies were both numerous and of large size. The majority were of the necrotic type; large circular cysts lined with flattened reticular cells and containing necrotic flakes of eosin-staining substance. Many had undergone beginning calcification. There were present also irregular cell complexes, formed by the fusion of large reticular cells, and in one section an enormous oval giant cell, with finely reticulated cytoplasm and an agglomeration of oval pale-staining nuclei at one pole of the cell mass.

The interesting and suggestive feature in this case is the extensive destruction of the small thymus cells. The other histological findings point merely to a somewhat premature involution of the gland—possibly the result of the hunger and privation to which the subject had been exposed several months before his death. It is tempting to attribute a special significance to the extreme disintegration of the thymus cells.

Case II.—A colored female domestic; 19 years of age; three months pregnant; died suddenly after an altercation with her lover. At the necropsy no signs of violence or poisoning were found; the woman exhibited, however, a marked Status lymphaticus.

The thymus in this case weighed 20 grams, extending downwards well beyond the auricles. On section, the thymic tissue was beefy red, glandular and soft, with very little fat.

Microscopically, the thymic tissue was moderately abundant, the lobules regular in shape and sharply delineated from the interstitium. The differentiation into cortical and medullary zones was fairly distinct and the cortex showed in places a distinct follicular arrangement. In other places there appeared to be a rarefaction of the small cells in the cortex, the marginal and reticular elements appearing more prominently than normal. In the medullary portions of the lobules the reticular epithelial cells prevail. The septa are broad, the fatty tissue more abundant than was evident in the gross. The oxyphilic cells are quite numerous, and are found also within the lobules. The Hassall bodies occur both as small concentric structures and as the large necrotic cysts. There are also many irregular hypertrophic cell complexes showing no definite concentric arrangement.

Under high magnification, the small thymus cells show pycnotic changes, extrusion of nuclear particles and fragmentation, but not to the same degree or extent as in the first case. Many of the small cells possess normal rounded nuclei showing no disintegrative changes. Phagocytosis, as in Case I., was not much in evidence. Occasionally one or two small cells were found included within the reticular cells. The blood vessels were normal.

Here again, then, we find evidence of acute destruction of the small thymus elements. The process, however, is far less intense than in the first case, and less

marked than has been found in cases dying of other pathological conditions. The absence of phagocytosis on the part of the reticular elements is worthy of mention.

Case III.—An Italian female; about 25 years of age; died several hours after taking some medicine to relieve "faintness." Analysis of the fluid showed no poisonous constituents. The necropsy showed intense congestion of all the viscera, including the intestinal tract, but no characteristic lesions of poisoning. There was, however, a pronounced Status lymphaticus.

The thymus weighed 32 grams and was glandular on section. Microscopic examination showed an abundance of parenchymal tissue in the form of sharply circumscribed lobules, separated by fairly broad septa of hyaline fibrous tissue and fat. There was no invasion of the lobules by connective tissue. Many granular oxyphilic cells were found in the stroma. The small thymus cells again showed marked fragmentation and pycnosis, especially in the central portions of the lobules. Phagocytosis could not be definitely made out.

Again, we have as the only striking variation from the normal, pronounced degenerative changes in the small cells. Otherwise the thymus presents the picture of normal or perhaps slightly delayed involution.

Case IV.—Male; 20 years of age; boxing with a friend, suddenly collapsed, dying six hours later. Previous health good. Necrosy disclosed chronic aortic disease and marked signs of Status lymphaticus. In spite of the presence of the stenotic aortic valvular lesion, the manner of death and the absence of previous symptoms suggest that the lymphatic state played a part in causing the sudden exitus.

The thymus weighed 50 grams, and was fleshy on section. Microscopically, there was a moderate amount of parenchyma, separated, however, by abundant adipose tissue. The lobules were irregular in shape and the normal differentiation into cortex and medulla for the most part wanting. The glandular substance was infiltrated with extensive hemorrhages. There was considerable invasion of the lobules by connective tissue (Heidenhain-Van Gieson). The small thymic cells were of unusually small size, their nuclei dense and diffusely stained. Fragmented and budding forms were, however, very scare. The reticular elements were well preserved. Phagocytic cells were scarce. There were noted several large multinuclear giant cells, enclosing a few small cells in their vacuolated cytoplasm. The Hassall bodies were large and almost exclusively of the necrotic type.

In this case, therefore, there is no evidence of an acute destruction of the glandular substance. The changes noted are characteristic of previous accidental involution.

Case V.—Male; about 30 years of age; found unconscious in cellar. No anatomical cause of death shown by necropsy. Status lymphaticus not marked.

Thymus 28 grams. Microscopically, thymic tissue is not abundant, much interlobular fat. Thymus lobules sharply circumscribed, cortex and medulla fairly well differentiated. No pycnosis or fragmentation of the small cells. There are numerous large necrotic Hassall bodies and extensive irregular areas of necrosis. Save for these necrotic areas, the gland may be considered normal for the age of the individual.

It will be seen from a review of the findings in these five cases of "idiopathic" death associated with Status lymphaticus that there is nothing which might be considered a typical feature. An extensive pycnocis and fragmentation occurred in but two of the cases. In none of them did the histological picture suggest a hyperfunctionating gland, or afford any basis for the theory that the sudden death in these cases is associated with an excessive secretion; on the other hand, well advanced involutional changes were present in three of the five cases.

Unfortunately, our material included no uncomplicated cases of "mors thymica" in childhood, save possibly the following:

Case VI.—Male infant; 8 hours old; found dead in bed with mother. Overlying suspected. Necropsy showed indications of asphyxia (multiple ecchymoses), and an unusually large, thick thymus weighing 61 grams. No compression of the trachea could be demonstrated.

Microscopically, the gland presents the normal appearance for a new-born infant. The small cells are well preserved, shows a distinct nucleolus and nuclear network, and there are occasional mitoses. The mononuclear oxyphilic cells are very abundant, both within the lobules and in the stroma about the vessels.

Dudgeon (58) has examined the thymus in fifteen cases of "thymic death" in children under 2 years. The average weight in this series is given as 25.11 grams. The structure of the glands in these cases was found to be normal save for the presence of large numbers of "eosinophile" cells, principally of the mononuclear variety. A detailed histological description of his cases is not given.

Schridde (59) considers a hyperplasia of the medulla, with thinning of the

cortex, as the characteristic feature of the thymus in status cases; also the presence of large degenerated Hassall bodies. He does not, however, state the nature of his material, nor cite specific cases in support of his views. Our own cases have not confirmed his findings.

(*b.*) *Diseases of the Ductless Glands*—The association of enlargement of the thymus with certain diseases of the ductless glands has been repeatedly noted. Very few of the reports include a detailed microscopic study of the thymus, and it may therefore be of interest to record the findings in our cases. The material included three cases of Basedow's disease, one of acromegaly and one of Addison's disease. All the cases presented a more or less marked grade of Status lymphaticus.

I shall first present briefly the findings in the three cases of Basedow's:

Case I. (Acc. No. 125).—Female; 23 years of age. Acute symptoms of Basedow's of ten weeks' duration. Death apparently from cardiac syncope.

Necropsy (*2* days post-mortem): Struma parenchymatosa. Status lymphaticus. The thymus was much enlarged, the two lobes together covering the pericardium; section, smooth and fleshy. Weight after dissection, 66 grams.

Microscopically, the gland consisted almost wholly of parenchymal tissue, traversed by rather dense fibrous septa. There is no distinct lobular structure, nor can one distinguish between cortical and medullary portions. There is, however, a differentiation in the form of irregular masses and strands of more densely packed cells, composed principally of reticular elements. The small cell-forms predominate. The nuclei are small, stain densely and diffusely (polychrome methylene blue eosin) and show no nuclear network or nucleolus. Their cytoplasm is usually scant, ragged, and strongly eosinophilic. Nuclear extrusions are abundantly present in places; some of these are connected by a narrow neck to the main body of the nuclear substance; others having undergone a slight change in their basophilic staining reaction lie free in the cytoplasm or adjacent to the cell in the intercellular spaces, where they appear to undergo solution. In addition to this process of nuclear budding or extrusion, occasional dumbbell forms are seen, suggesting amitotic division. Definite mitotic figures are not seen. The reticular epithelium under high magnification appears to be abundantly present. There are irregular fibrillary cell-complexes, isolated large cells with branching and anastomosing processes and more circumscribed oval cells, with vacuolated cytoplasm, lying free among the small cells. The last type especially appears to show active phagocytic properties towards the small cells. There are numerous small Hassall bodies, most of them containing a central necrotic mass with nuclear detritus. Calcification is not present. The stroma presents no noteworthy features. The rather dense fibrous septa contain occasional mast cells, but no oxyphilic cells. The blood vessels are thin-walled and congested. The rather numerous small lymphocytes within their lumen show no fragmentation or nuclear extrusions

The picture in this case is that of a very cellular and apparently actively functionating organ: the relative proportion of parenchyma and stroma corresponds to that of the thymus in very early childhood.

Case II.—Male; German; 55 years of age. Severe symptoms of exophthalmic goiter for past fifteen years. Treatment with Beebe's serum with marked improvement. Relapse after discontinuing treatment. Death occurred rather suddenly. The necropsy showed a parenchymatous goiter, exophthalmos, chronic interstitial nephritis, hydrothorax, follicular enteritis (?), hypertrophy and dilatation of the heart. In addition, there was a general and very pronounced hyperplasia of all the lymphoid structures.

The thymus measured 9 x 4.5 x 1.5 centimeters, appeared fleshy and showed a lobular structure on section. It weighed 27.5 grams. Microscopically, the thymic tissue was abundant, but divided into irregular lobules by a large amount of loose fibrous tissue and fat. The individual lobules were fairly well circumscribed; along their periphery were compact circular masses of small cells, limited by a circle of cells arranged evenly in a line; the appearance suggested that seen about a rapidly growing lymphoid follicle, but there were no germinating centres.

As in Case I., the prevailing type of cell was the "lymphoid" cell, but reticular epithelial cells and transitional cell forms were very numerous. The nuclei of the small cells show the same budding forms as in the previous case; many of the nuclei show radially arranged nuclear extrusions, so that they might be mistaken for astral mitotic figures. I could not persuade myself that true mitoses were present. Phagocytosis of the small cells by the reticular cells was not to be seen. The Hassall bodies were numerous, small, and frequently in the form of irregular cell-complexes. The blood vessels were relatively thin-walled and packed with red cells.

The findings in this case suggest a secondary hyperplasia in a partially involuted thymus. The follicular arrangement of the cortex indicates the presence of growth centres, and the compression of the surrounding small cells denotes a centrifugal growth. The proliferation of the small cells in these follicles apparently takes place amitotically; at least undoubted mitoses could not be detected. That a differentiation of the reticular cells into cells of the small type is also occurring, especially in the central zone of the lobules, is evidenced by the numerous transitional cell-forms. Again there was no reason to seek an extrinsic source for the small cells.

Case III.—Female; 45 years of age. Symptoms of exophthalmic goiter for past thirteen years. Died rather suddenly, apparently from cardiac syncope. Necropsy: Exophthalmic goiter; chronic interstitial nephritis; chronic valvular disease (aortic); coronary sclerosis; chronic interstitial oöphoritis. The lymph nodes are noted as being enlarged, but there is no definite record of Status lymphaticus.

The thymus is described as fatty, the weight not recorded. Microscopically, however, there are found many islands of thymic tissue, some attaining a diameter of 3 or 4 millimeters; the lobules are not circumscribed and are separated by abundant fat. There is no differentiation between cortex and medulla, the small cells being evenly distributed throughout the lobules. With the low power, one may, however, distinguish the large reticular cells standing out prominently among the small cells. Under high magnification, we again see the nuclear extrusions more marked even than in the other two cases. There appears to be also a hyperplasia of the reticular epithelium, the nuclei being large, containing a very distinct chromatin network, and showing occasionally amitotic divisional forms. The Hassall bodies are for the most part small, with central necrotic areas; the irregular cell-complexes and young concentric forms are also present. The large blood vessels show marked thickening of their adventitia; the capillaries are congested.

The presence of a so-called "persistent" thymus in the majority of cases of exophthalmic goiter, usually associated with general lymphoid hyperplasia and other evidences of the lymphatic state, is of interest from several points of view. The frequency of sudden deaths, especially during or immediately following an operative attack upon the thyroid, has been variously explained. Of late there has been manifested a tendency to lay the blame upon the associated enlargement of the thymus or the general lymphatic state (Boit (60), Hart (61), Capelle (62), Gierke (63), Hansemann (64), and others). A functional relationship between thyroid and thymus has been assumed by some on the basis of these almost constant findings. Moebius (65), believes that the presence of an enlarged thymus indicates that there is a congenital disposition to hyperthyroidism before the active symptoms of the disease are manifest.

It is not to be expected that the histological examination of the thymus in these cases will supply the answer to all these problems. One question, however, which should be decided by histological evidence is whether we have in the enlargement of the thymus merely a persistence of the infantile condition, that is, a congenital anomaly, part of the lymphatic constitution; or whether there occurs in these cases a secondary hyperplasia due to the influence of the disease. Indeed, a similar problem arises in the interpretation of the frequently associated lymphatic hyperplasia itself; is this, too, a congenital affair, or does it occur secondarily in connection with the disease? I would refer to a recent article of Bartel upon the significance of the "hypoplastic constitution" (Wiener Klin. Wochensch., 1908, No. 22) for a theoretical discussion of this interesting question.

The following considerations appear to justify the view that the thymus in these cases of Basedow's has undergone a renewal of growth, rather than "persisted" in its infantile condition. In Case I. the structure of the gland differs from that of the normal infantile thymus. The lobules are not sharply circumscribed, there is no distinction between cortex and medulla, there is no follicular arrangement of the small cells in the peripheral portion of the lobules. The oxyphilic cells, usually numerous during early life, are wanting. In the involuted organs of Cases II. and III. the signs of regeneration are still more unmistakable. When we consider that the patients did not develop symptoms until the age of forty, a period at which the thymus tissue is normally very scant and composed chiefly of reticular elements, the conclusion seems inevitable that there has been a renewed growth of thymus tissue, and not merely a persistence. The conclusion is backed up by the structural differences between these organs and the uninvoluted or partially involuted thymus.

Assuming then that there has been a renewed growth, what is the origin of the small cells forming the bulk of the glands? This brings up again the question of the normal histogenesis of the small cells. The advocates of the lymphocytic nature of these cells would claim that they were brought to the gland through the lymph

channels, possibly undergoing further multiplication in situ; or that they migrated through the walls of the blood vessels. Those believing in their epithelial nature would conceive of two possibilities; either they arise through the repeated division of small cells already present or through a renewed differentiation of the reticular cells into cells of the small type. The question is of such importance for an understanding of the general pathology of the organ that it requires a minute analysis.

In favor of the first view I can find in these cases no histological evidence. The endothelial lined clefts in the fibrous septa and capsule are small, and do not contain many lymphocytes; neither are there found lymph spaces crowded with lymphocytes within the lobules. Nowhere are there accumulations of lymphoid cells in the perivascular lymphatics. It seems incredible to me that the enormous number of small cells should have been carried to the thymus from without via the lymphatic channels.

In Case I. the blood vessels contained a somewhat increased number of lymphocytes. This we should expect in view of the usual occurrence of an absolute and relative lymphocytosis in Basedow's disease. I have never, however, seen a migration of lymphocytes through the capillary wall, nor is it believable that this occurs on a sufficiently large scale to account for all the small cells within the lobules.

In this connection Rudberg's (22) study of the regeneration of the thymus in rabbits following Röntgenization is of interest. He found that within three and one-half hours following exposure there is marked disintegration of the small thymus cells, the nuclear fragments being taken up by the reticular epithelium or dissolved in the intercellular spaces in from twelve hours to two days; according to the length and intensity of the exposure there may be a complete disappearance of the "lymphoid elements," the gland taking on an epithelioid character. The degeneration of the reticular epithelium takes place later and continues after the small cells have begun to regenerate. During the regenerative process the thymus cells appear first in the central (medullary) portion of the lobules; later they are evenly distributed, and finally they are again most numerous in the peripheral zone and the lobules reassume their original appearance. Mitoses occur almost exclusively in the reticular cells. During the later stages of regeneration (ten to nineteen days) there is a marked invasion of polynuclear leucocytes (pseudo-eosinophiles) derived from the blood. There are found, even in the early stages, collections of lymphoid cells in the interstitium and in the perivascular spaces about the intralobular vessels.

The small cells which Rudberg believes with Hammar to be true lymphocytes he assumes are brought to the thymus from the neighboring mediastinal lymph nodes, a view which would involve the assumption that there took place a reversal in the normal lymph current. Their first appearance in the central portion of the lobules he explains by their being conveyed along the perivascular lymphatics. He does not believe that they are derived either from the blood vessels or from the reticular epithelium. Rudberg's interpretation of his findings appear to me to be colored by his evident desire to support Hammar's belief in the lymphocytic nature of the small thymus cells. His illustrations (Tafel II., Fig. 14) depict groups of small cells lying in spaces bounded by connective tissue fibrils, but the endothelial lining, if present, is not shown, and it appears to be highly questionable whether these are really lymph spaces. The first appearance of the small cells during regeneration in the central portion of the lobules is difficult to explain; one would expect to find them principally in the septa and peripheral portions, that is, at the points of entrance of the lymphatics. The few collections of lymphocytes in the septa may well be inflammatory in origin, since there is a simultaneous appearance of polynuclears. Finally, the early appearance of mitoses in the reticular epithelium suggests a participation of these elements in the restoration of the organ.

The question, therefore, cannot be said to have been decided by Rudberg's interesting study, and the origin of the small cells during regeneration of the gland has not, so far as I know, been considered by other writers. My own conviction is that the small cells may arise either through the multiplication in situ of pre-existing small cells or through a differentiation of the proliferating reticular epithelium. The presence of numerous transitional forms in the Basedow thymus above described is very suggestive. Many of the otherwise typical small cells possesses long protoplasmic processes, some of which undoubtedly anastomose with the reticular epithelium. Many cell-forms with small densely staining nuclei but abundant irregular eosin-staining cytoplasm, cannot be classified either as cells of the reticular or lymphoid type. The presence of such intermediate cell-forms in large numbers points to an active differentiation of reticular cells into cells of the so-called lymphoid type; and the anatomical connection between the two kinds of cells adds confirmation to Stohr's theory as to the epithelial nature of the small cell. If this view as to the origin of the small cells from the reticular epithelium be correct it follows that the

hyperplasia of the thymus in Basedow's disease cannot be considered a part of the general lymphoid hyperplasia so often present in these cases. It represents, on the other hand, a specific reaction of the thymus in this disease, in all probability associated with an excess of function. I have already expressed the view that the extrusion of nuclear particles by the nuclei of the small cells may indicate a secretory function on the part of these cells. If this be true we have in the thymus of these cases histological evidence of an excessive secretory activity.

In view of the recent publications of Wiesel (66), Hedinger (67) and Hart (68), calling attention to the frequent correlation of Addison's disease with "persistent" thymus and general evidences of Status lymphaticus, a record of our findings in the single case available for study is of interest. In the cases recorded no detailed description of the histological appearance of the thymus is given, and it has been tacitly assumed by all save Hart that the thymic enlargement is merely one feature of the general lymphatism. Hart, however, believed that there occurred in the thymus of his case a secondary hyperplasia in an already involuted organ. His theoretical explanation of this phenomenon does not concern us here.

Hart's case was a 23-year-old female with symptoms of Addison's extending over three years. Necropsy: complete fibro-caseous degeneration of both adrenals; arterial hypoplasia; hyperplasia of thymus and general lymphadenoid tissue.

The thymus weighed 39 grams, and was thick and fleshy. It is described as consisting almost entirely of "lymphatic" elements, which are divided into islands by narrow fatty and fibrous septa, without distinct lobulation. The fat cells are separated by narrow strands of lymphocytes which indicated proliferation rather than persistence. The Hassall bodies were strikingly few in number. Some were well preserved, others necrotic.

Our own case also illustrates the association of a "persistent" thymus and Status lymphaticus with Addison's disease.

H. G.; female; 32 years of age. Typical history of Addison's disease. Death occurred with symptoms of extreme asthenia and emaciation.

Necropsy: diffuse pigmentation of skin; patchy areas of pigmentation in mucous membranes. Tuberculosis of both adrenals with complete destruction of medulla and only microscopic rests of cortical substance; tuberculous spondylitis. General lymphoid hyperplasia. Arterial hypoplasia.

Thymus large, 10 grams, 9 x 2.5 x 1.5 centimeters. The gland consists of irregular but sharply outlined lobules separated by abundant adipose tissue. Individual islands attain a diameter of 3 to 4 millimeters. In the large lobules the differentiation between cortex and medulla is fairly distinct, and there are here and there denser aggregations of small cells in the form of spherical "follicles." The cortical portions of the lobules are occupied chiefly by small cells with irregular cell outlines. The nuclei appear slightly larger than those of the lymphoid cells, and in well differentiated Heidenhain hematoxylin preparations show a distinct nucleolus and sharply defined nuclear membrane. Between the small cells are found occasional reticular cells with large pale oval nuclei and branching cell processes. The medullary portion of the lobules contains cells of both types, the small cells being relatively numerous. Typical concentric Hassall bodies are not abundant; hypertrophic cell-complexes showing a beautiful fibrillary differentiation are fairly numerous. The intralobular capillaries are thin walled and packed with red cells. The stroma consists principally of adipose tissue and contains very few other cellular elements. Mast-cells are seen in unusual numbers; oxyphilic cells, either with or without definite granulæ, are wanting.

In a general way the structure of the thymus in this case approximates the normal findings in the thymus of a twenty-year-old individual (cf. Hammar, Fig. 9). This is the more remarkable in view of the extreme cachexia and general visceral atrophy shown by the subject. The abundance of thymic tissue is therefore distinctly abnormal. The same question, however, arises as in the case of the enlarged thymus associated with Basedow's disease: have we a mere persistence of the organ, correlated with a coincident lymphatic constitution; or has there been a secondary growth of thymic tissue in an already involuted organ? The latter seems to me the more probable, although the histological evidence is less conclusive than in the case of the thymus enlargement associated with Basedow's disease. The occurrence of closely packed follicles of small cells suggests active multiplication; the numerous reticular epithelial cell-complexes also suggest an increase in these elements. Mitoses were not found. The extrusion of nuclear particles by the small thymic cells, so conspicuous in the thymus of the exophthalmic goiter cases, was not a pronounced feature. Finally, it is to be noted that the lesions of "accidental involution," as we shall have occasion to describe them more fully later, were conspicuously wanting, in spite of the severe emaciation and the chronic tuberculous lesions. There was no

invasion of the lobules with connective tissue; the lobular outlines were distinct, and the stroma free from cellular infiltration. The reason for this exceptional condition I am unable to suggest.

The frequent association of enlarged or persistent thymus in acromegaly has been emphasized by Sternberg (69) and others.

The single case in which I have had the opportunity to study the thymus was that of a male 38 years of age, who had shown symptoms of brain tumor and acromegaly for four years. There was diabetes for last two years of life.

Necropsy: acromegalic lesions of osseous system; general splanchnomegaly; very large adenoma of the hypophysis, invading frontal lobes; sclerosis and hyaline degeneration of the Islands of Langerhans; Status lymphaticus.

The thymus was very greatly enlarged, extending from thyroid to base of ventricle. It weighed 70 grams. Microscopically, the abundant thymic tissue was arranged in the form of circumscribed, rather closely apposed irregular lobules. The interstitial tissue is composed principally of fat and hyaline connective tissue, in which are streaks and agglomerations of small cells. With the naked eye there is distinct differentiation between cortex and medulla, due to the closer aggregation of the small cells in the periphery of the lobules. The small cells show very numerous budding forms and nuclear extrusions—appearances which we have ventured to interpret as evidences of active functionation. There are also many diplococcal and dumb-bell forms, suggesting direct division. The nuclei of the reticular cells are unusually large and rich in chromatin, and many transitional forms are found. The Hassall bodies are for the most part small, with necrotic centres, and show no striking features. Oxyphilic cells are not found.

This case has been reported in detail by Dr. Charles Norris; see Trans. N. Y. Path. Soc., New Series, Vol. VII., No. 1, 1909; also Bellevue Hospital Reports, 1908.

CONCLUSIONS.

The histological features in the thymus associated with the above diseases of the ductless glands may be summarized as (1) active proliferation of the thymic elements and (2) absence of regressive changes. The picture in the individual cases is modified by the grade of involution previously present; in all cases the amount of thymic tissue is greatly in excess of that normally present at a corresponding age. In all the cases examined, nuclear extrusions were abundantly present, indicating, in our opinion, a functional hyperactivity. The absence of oxyphilic cells is also noteworthy.

(*c.*) *Congenital Syphilis*—The literature upon the syphilitic changes in the thymus is not extensive. The cysts sometimes found in the thymus of children afflicted with hereditary syphilis, known after their discoverer as Dubois abscesses, were found by Chiari (70) not to be abscesses but epithelial lined cysts filled with small thymus cells, which occurred but seldom in the normal thymus. Eberle (71), investigating these cysts, found them filled with true pus, and interpreted them as rests of the thymic lumen. Tuve (72) atributed the cyst formation to a necrosis of the medullary substance. Simmonds (43) in a recent article considers the cyst formation as a specific syphilitic lesion, because of the finding of spirochetæ in great numbers within the cyst cavities. He also emphasizes the epithelioid appearance of the thymus in these cases and interprets the picture as an arrested development.

I have not made an extended study of the thymus in congenital syphilis. The two cases examined were, however, in many respects remarkable.

The first was obtained from a seven months' macerated fetus, and was impregnated according to Levaditi's method, using polychromo methylene blue as counterstain. The sections showed innumerable very typical spirochetæ pallidæ in every field; the individuals formed here and there tangled clusters, suggesting post-mortem multiplication. They were present everywhere, but especially numerous in and about the walls of the blood vessels. There could be distinguished cystic spaces filled with necrotic detritus, but the spirochetæ were not more densely crowded in these cysts than elsewhere. On the basis of this, taken with the fact that similar cystic spaces could be demonstrated in other cases in which there was no suspicion of syphilis, I am inclined to doubt the statement of Simmonds that these cysts are caused by Spirocheta pallida and are characteristic syphilitic lesions.

Although the finer structural details could not be made out because of the poor state of preservation, one could detect certain very striking features. One of these was the very marked increase in the perilobular connective tissue, compared with the normal gland at the corresponding age. This indicates conclusively that the effect of the congenital syphilitic infection, in this case at least, is not merely an arrest of development but an actual atrophy or degeneration of the gland with replacement fibrosis. A second noteworthy alteration was the partial disappearance of the small

thymus cells and the presence of large numbers of polyhedral and pyramidal epithelial cells; in all probability representing the undifferentiated reticular epithelium. These large cells frequently contained granulæ and red-shaped bodies impregnated with silver and possibly representing the fragments of degenerated spirochetæ. The intact spirochetæ, though frequently lying upon the surface of these cells, do not appear to be phagocytosed by them.

The second case studied was also highly interesting. The thymus was taken from a well-nourished eleven weeks old syphilitic infant, showing a general purpuric eruption, interstitial pneumonia, and a well marked Status lymphaticus. The thymus was large and infiltrated with diffuse hemorrhages. It weighed 25 grams. Microscopically, it was found to consist almost wholly of large reticular epithelial cells, with indefinite cell outlines and extensive intercellular connections (Fig. 4). The intercellular fibrils though not numerous were very distinct and clearly demonstrable with the Mallory phosphotungstic hematoxylin stain. The nuclei were very large, vesicular, rarely showing a distinct nucleolus. The chromosomes were in the shape of short bulbous rods and tended to lie against the nuclear membrane. Pyriform extrusions of chromatin were present in some of the cells (Fig. 4), and small threads and rods of chromatin-staining substance were found free within the cytoplasm. The cytoplasm of the reticular cells was spongy in appearance, and not infrequently contained yellowish pigment granules, probably hematogenous. Typical mitoses were very numerous. Small thymus elements were very scarce, and many of them showed direct protoplasmic connections with the reticular epithelium; they showed no definite arrangement, but were scattered between the large epithelial cells.

The most striking feature of the gland was the complete absence of lobular structure. Aside from the connective tissue in the capsule, and in the considerably thickened adventitia of the larger blood vessels, the organ was entirely free from connective tissue and the characteristic septa were wanting. The tissue, therefore, presented a homogeneous structure, both in the gross and under the microscope. A further remarkable feature was the entire absence of Hassall bodies, or the irregular cell-complexes which we have learned to recognize as the forerunners of these structures. Furthermore, the oxyphilic cells, normally abundant at this age, were not to be found.

The entire gland was infiltrated with diffuse hemorrhages; to these must be attributed the extensive areas of necrosis, which were present. Cyst formation was not present either in the gross or microscopically. The search for spirochetæ pallidæ in Levaditi sections was unsuccessful.

The structural features in this case suggest an arrest of development, or rather a failure of the gland to undergo its customary differentiation. Essentially, the gland resembles that of a very early stage of development before the ingrowth of blood vessels has given to the organ a lobular structure. A study of further material is necessary before deciding whether this is a frequent manifestation of syphilis in early life. The thymus from a fifteen-year-old boy dying of juvenile paresis upon an hereditary syphilitic basis failed to show similar changes.

(*d.*) *Acute and Chronic Infections and Wasting Diseases*—One of the most interesting facts about the thymus is its extreme sensitiveness to toxic agencies of various sorts. So manifest and striking is this reaction that it marks the thymus as an organ apart. Although the extreme and rapid reduction in the weight and volume of the thymus occurring in the course of general infections was known to Friedleben, and although numerous writers have depicted the atrophic fibrous gland which is seen in marantic conditions, little attention has been paid to the intimate histological changes involved in these regressive processes, and especially to the changes found in acute infections. This is the more remarkable since one would expect a priori that the abrupt reduction in the amount of thymic parenchyma would be disclosed in the histological picture, and that one would find at all times the signs of extensive disintegration of the thymic elements.

Before presenting our tabulated cases and the conclusions derived from our own study it is necessary to refer briefly to some of the more important contributions to this chapter of the subject. Hammar (18) has described under the term "accidental involution" the general alterations in the structure of the thymus following infections and toxic conditions, but is concerned chiefly with the modifications in the architecture of the organ. His study is based upon eighty cases of disease, including acute and chronic infections and chronic wasting diseases. His general conclusions are as follows: The "lymphoid" elements are first affected in the process of accidental involution, becoming less numerous and finally disappearing. The reticular cells degenerate later. There is a reduction in the total parenchymal substance in all cases. There is no increase in

the absolute weight of the connective tissue, nor does a true proliferation take place. The connective tissue, however, becomes more compact and firm. Fat cells appear at an age when they are not normally present in the thymus. Accidental involution never leads to a complete disappearance of the parenchyma. A narrowing of the cortex or a complete disappearance is characteristic; in all cases the demarcation between cortex and medulla becomes obscured. In some cases the number of small cells within the medulla appears increased. The follicular arrangement of the cortical cells is lost. The boundary between parenchyma and interstitial tissue also becomes less sharply defined, the interstitium becoming more cellular. This is due to an extensive emigration of the "lymphoid" cells into the interstitial tissue. The Hassall bodies may show an apparent increase, because of the rarefaction of the intervening substance. In the later stages of accidental involution they may disappear completely.

Roger and Ghika (73) have found that the thymus reacts to spontaneous and experimental infections and intoxications by assuming a vicarious hematopoetic function. They were led to this erroneous belief by finding granular eosinophiles, mast cells, and myeloplaques (?) in these cases.

Francesconi (74) has studied experimentally the effects of acute and chronic bacterial infections upon the thymus of guinea-pigs and rabbits. His descriptions are based upon the text-book conception of the thymus as a lymphatic gland plus Hassall bodies. In acute infections, especially after injections of pneumococci and diphtheria bacilli, he noted swelling of the gland, proliferation of the lymphatic elements especially in the medulla, karyolytic changes in the nuclei (of the small cells?), phagocytosis of bacteria by macrophages, swelling of the capillary endothelium, and round cell infiltration of the stroma.

In subacute and chronic infections there was marked atrophy of the gland with proliferation of the inter- and intra-lobular connective tissue. In a case of diphtheria in a child the same changes were found as in the experimental infections, but the thymus is described as reduced in weight. In pneumonia, on the other hand, he found the thymus increased in weight. No figures are given, however, and this observation requires further confirmation.

Another writer who has investigated the pathological histology of the thymus on an extended scale is Dudgeon (58). His descriptions are also based upon the text-book conception of the thymus as a lymphoid organ with a fibrous reticulum. His material included few adult cases, and the minute histological details are largely omitted. His results, however, are of value in substantiating the view that there is a marked reduction in the parenchymal substance both in acute and chronic disease.

In acute diseases of various kinds Dudgeon found the average weight to be only 5.4 grams, approximately one-fifth of the normal average, if we accept the statements of Friedleben, Hammar, and the writer. His histological descriptions refer only to the presence of fibrosis, hemorrhage, calcification of the Hassall bodies, and to the presence of eosinophile cells. In many of his acute cases the gland is described as normal, and no clue is afforded as to the manner in which the striking reduction in the weight of the gland is brought about.

In "primary atrophy" of the thymus associated with marasmus, Dudgeon found a still more marked reduction in the average weight of the thymus (maximum five grams, minimum .9 gram). The lesions are described simply as a sclerosis with rarefaction of the cortex, and differ only in degree from those present in the marantic stage of tuberculosis or other chronic diseases.

Fortescue-Brickdale (75), in his study of the thymus in infancy, finds similar fibrotic changes in acute and chronic disease. Stokes, Ruhrah and Rohrer have also investigated the pathology of the thymus in infantile marasmus. The average weight in sixteen cases was only 2.2 grams, or approximately one-tenth of the normal average for the first five years of childhood (Hammar). The lesions found are described as a marked inter- and intra-lobular sclerosis, together with a hyaline degeneration of the Hassall bodies. They describe the large necrotic cystic forms. The lesions in the cases of secondary atrophy from tuberculosis were essentially the same.

Lucien (76) and Lucien and Parisot (77) found similar changes in the thymus of marasmus cases, and showed that the atrophy is out of proportion to the general loss of body weight. Whereas normally the relation ranges between 1 to 260 and 1 to 1400, in marasmus the average ratio was 1 to 7722.

Among other writers who have called attention to precocious involution of the thymus in marantic states are Durante (78), Farret (79), Mettenheimer (80), Dvornitschenko (81), and Bovaird and Nicoll (51).

Our own observations upon the thymus in cases of infectious disease and chronic wasting disease are presented herewith in tabulated form.

r Epithelium.	Hassall Bodies.	Blood Vessels.	Remarks.
ion.)	Very numerous; many large necrotic forms, with marked calcification.	Congestion.	
generation; pha- narked.	Numerous small cell complexes and necrotic forms with calcification.	Congestion. Contain many polynuclear leucocytes.	Acute degenerative changes.
generation; pha- narked.	Not numerous; small cell complexes and necrotic forms.	Congested; some contain polynuclear leucocytes and hyaline thrombi.	Acute degeneration. Diffuse hemorrhages into parenchyma.
vacuolar degen- xtreme phagocy-	Very numerous; large epithelial cell complexes.	Congested.	Advanced degeneration.
generation; pha- light.	Not numerous, small, necrotic.	Marked thickening of adventitia.	Early acute degeneration.
		Congested.	
vacuolar degen- phagocytosis.	Irregular and concentric cell complexes. No necrotic Hassall bodies.	Congested.	Marked acute degeneration.
thelium well pre- agocytosis slight.	Numerous cell complexes; also large necrotic Hassall bodies with calcification.	Congested. Swelling of endothelium.	Advanced acute degeneration.
ithelium shows rative changes. is?	Numerous, small, necrotic.	Intense congestion. Diffuse hemorrhages into parenchyma.	Advanced acute degeneration. Early involutional changes.
cuolar degenera- narked phagocy-	Fairly numerous, necrotic, with extensive calcification.	Diffuse sclerosis.	Normal involution, with acute degeneration.

Acute and Chronic Infections.

Name or Acc. No.	Sex.	Age.	Anatomical Diagnosis.	Status Lymph.	Weight of Thymus.	Duration of Illness.	Amount of Thymic Tissue.	Shape of Lobules.	Differentiation of Cortex and Medulla.	Predominant Cell Type.	Interstitium.	Small Thymus Cells.	Reticular Epithelium.	Hassall Bodies.	Blood Vessels.	Remarks.
749.....	M.	44 years.	Epidemic cerebro-spinal meningitis.	+++	68 grams.	4 days	Very abundant.	Regular, circumscribed, closely apposed.	Absent.	Small cells, both medulla and cortex.	Scant, fibrous, not cellular; slight fatty invasion of lobules; oxyphilic cells(?); karyorrhexis of connective tissue nuclei.	Marked pycnosis and karyolytic changes.	? (Thick section.)	Very numerous; many large necrotic forms, with marked calcification.	Congestion.	
868.....	M.	5 years.	Epidemic cerebro-spinal meningitis.	+++	28 grams.	1 day.	Abundant.	Regular, circumscribed.	Well marked; follicular cortex.	Small cell.	Fairly abundant, fibrous; in places groups of small cells (lymphocytes?); no oxyphilic cells.	Nuclear extrusions, pycnosis and fragmentation marked	Vacuolar degeneration; phagocytosis marked.	Numerous small cell complexes and necrotic forms with calcification.	Congestion. Contain many polynuclear leucocytes.	Acute degenerative changes.
748.....	F.	12 years.	Epidemic cerebro-spinal meningitis.	++	31 grams.	2 days.	Very abundant.	Regular, circumscribed.	Distinct; some rarefaction of cortex.	Small cells.	Not abundant; loose fibrous tissue and fat; few polynuclear eosinophiles.	Nuclear extrusions, pycnosis and fragmentation marked.	Vacuolar degeneration; phagocytosis marked.	Not numerous; small cell complexes and necrotic forms.	Congested; some contain polynuclear leucocytes and hyaline thrombi.	Acute degeneration. Diffuse hemorrhages into parenchyma.
881.....	F.	5 years.	Epidemic cerebro-spinal meningitis.	++	?	2 days.	Abundant.	Regular, fairly circumscribed	Indistinct; rarefaction of cortex; marginal layer distinct; many small cells in medulla.	Reticular cells.	Fairly abundant, fibrous tissue; no fat; no oxyphilic cells	Nuclear extrusions, pycnosis and fragmentation marked in places	Very marked vacuolar degeneration; extreme phagocytosis.	Very numerous; large epithelial cell complexes.	Congested.	Advanced degeneration.
553.....	M.	10 years.	Acute sphenoiditis (meningococcus).	++	26 grams.	18 hours.	Very abundant.	Regular, fairly circumscribed.	Distinct; follicular cortex.	Mixed.	Hyaline fibrous tissue; few fat cells; many oxyphilic cells in stroma and within lobules.	Slight pycnosis and fragmentation.	Vacuolar degeneration; phagocytosis slight.	Not numerous, small, necrotic.	Marked thickening of adventitia.	Early acute degeneration.
341.....	M.	30 years.	Epidemic cerebro-spinal meningitis.	++		4 days.	Not abundant.	Irregular strands and lobules.	Indistinct.	Reticular cells.	Abundant, fatty, few cellular elements.				Congested.	
1907.....	F.	3 days.	Hemorrhagic disease of the new-born.	0	75 grams.	3 days.	Very abundant.	Regular, circumscribed.	Distinct.	Cortex, small cells; medulla, mixed.	Thin fibrous septa; numerous oxyphilic cells.	Moderate pycnosis and fragmentation	Very marked vacuolar degeneration and phagocytosis.	Irregular and concentric cell complexes. No necrotic Hassall bodies.	Congested.	Marked acute degeneration.
1582.....	M.	27 years.	Laryngeal diphtheria (Sudden death during intubation).	0	25 grams.	Few days.	Abundant.	Irregular, not circumscribed.	Absent.	Mixed; small cells evenly distributed throughout lobules.	Edematous fibrous tissue and fat, invading lobules; fairly numerous oxyphilic cells within lobules.	Nuclear extrusions, pycnosis and fragmentation very marked.	Reticular epithelium well preserved; phagocytosis slight.	Numerous cell complexes; also large necrotic Hassall bodies with calcification.	Congested. Swelling of endothelium.	Advanced acute degeneration.
954.....	M.	23 years.	Lobar pneumonia.	++	60 grams.	6 days.	Abundant.	Irregular, fairly circumscribed.	Absent.	Mixed; small cells distributed throughout lobules.	Abundant fat and loose, edematous fibrous tissue, invading lobules; few granular oxyphilic cells within lobules.	Nuclear extrusions; no marked fragmentation.	Reticular epithelium shows no degenerative changes. Phagocytosis?	Numerous, small, necrotic.	Intense congestion. Diffuse hemorrhages into parenchyma.	Advanced acute degeneration. Early involutional changes.
837.....	M.	35 years.	Lobar pneumonia; pneumococcussepsis.			?	Not abundant.	Irregular, fairly circumscribed.	Absent.	Mixed; sharply circumscribed nests of reticular epithelium.	Abundant, principally fat; few granular oxyphilic cells within lobules.	In places marked pycnosis and fragmentation.	In places vacuolar degeneration with marked phagocytosis.	Fairly numerous, necrotic, with extensive calcification.	Diffuse sclerosis.	Normal involution, with acute degeneration.

Epithelium.	Hassall Bodies.	Blood Vessels.	Remarks.
ive changes; no s.	Numerous, small, necrotic.	Congested; marked adventitial thickening.	Advanced acute degeneration, with beginning involutional changes.
ive changes; no s.	Small cell complexes and necrotic forms; cysts lined with single or multiple layer of epithelial cells.	Larger arteries show hypertrophy of all coats; no degenerative changes.	
uolar degenera- te phagocytosis.	Not numerous; cell complexes and small calcareous forms.	Slight adventitial thickening; marked fibrin network.	Acute degeneration, with chronic fibrosis and atrophy.
ve changes; no s.	Few small cell complexes and necrotic forms.	Slight adventitial thickening.	No acute degeneration; "marked accidental" involution.
ve changes; no .	Very numerous large sequestra, with beginning calcification.	Marked sclerosis.	Advanced "accidental" involution.
ve changes; no .	Small cell complexes; few small necrotic forms and cysts.	Normal.	Normal gland. Probably idiopathic "status" death.
licles reticular acuolar degen. hagocytosis.	Small cell complexes and necrotic forms.	Swelling and proliferation of endothelium; hyaline degeneration of capillary walls.	Acute degeneration upon chronic involutional changes.
ve changes.	Numerous hypertrophic cell complexes and necrotic Hassall bodies.	Slight sclerosis.	Congenital involutional changes.
eration, many id vacuolated ll s; moderate	Numerous cell complexes and small necrotic forms; no large sequestra.	Slight hyaline degeneration; marked proliferation of adventitia.	Advanced acute degeneration, with beginning fibrosis.

Acute and Chronic Infections.

Name or Acc. No.	Sex.	Age.	Anatomical Diagnosis.	Status Lymph.	Weight of Thymus.	Duration of Illness.	Amount of Thymic Tissue.	Shape of Lobules.	Differentiation of Cortex and Medulla.	Predominant Cell Type.	Interstitium.	Small Thymus Cells.	Reticular Epithelium.	Hassall Bodies.	Blood Vessels.	Remarks.
1304.....	M.	17 years.	Suppurative osteomyelitis; pyemia.	++	?	11 days.	Fairly abundant.	Irregular; poorly circumscribed.	Absent.	Mixed.	Abundant; fat and hyaline connective tissue; marked invasion of lobules; occasional oxyphilic cell within lobule.	Slight fragmentation.	No degenerative changes; no phagocytosis.	Numerous, small, necrotic.	Congested; marked adventitial thickening.	Advanced acute degeneration, with beginning involutional changes.
1855.....	F.	6 years.	Lobar pneumonia; glomerulo-nephritis.	++	11 grams.	2 weeks +.	Fairly abundant.	Regular; well circumscribed.	Poorly marked; marginal zone distinct.	Mixed; small cells distributed throughout lobules.	Abundant; loose fibrous tissue and fat; oxyphilic cells very numerous, both in stroma and within lobules.	Very slight fragmentation or pycnosis; small cells show distinct nuclear structure.	No degenerative changes; no phagocytosis.	Small cell complexes and necrotic forms; cysts lined with single or multiple layer of epithelial cells.	Larger arteries show hypertrophy of all coats; no degenerative changes.	
2103.....	M.	24 years.	Pneumococcus sepsis.		11.5 grams.	2 weeks +.	Fairly abundant.	Irregular; not circumscribed.	Absent.	Mixed; many small cells in medulla; marginal zone very distinct.	Abundant; edematous fibrous tissue and fat; slight intralobular sclerosis; no oxyphilic cells; many mast cells.	Intense fragmentation and pycnosis.	In places vacuolar degeneration; moderate phagocytosis.	Not numerous; cell complexes and small calcareous forms.	Slight adventitial thickening; marked fibrin network.	Acute degeneration, with chronic fibrosis and atrophy.
1844.....	F.	20 years.	Chronic and acute verrucous endocarditis; acute pericarditis.	+++	?	2 weeks +.	Not abundant.	Very irregular; not circumscribed.	Absent.	Spindle-shaped reticular cells.	Abundant; fatty with few dense fibrous strands; few granular oxyphilic cells, chiefly within lobules; numerous mast cells.	Well preserved; in places slight fragmentation and nuclear extrusions; free nuclear particles.	No degenerative changes; no phagocytosis.	Few small cell complexes and necrotic forms.	Slight adventitial thickening.	No acute degeneration; "marked accidental" involution.
665.....	M.	18 years.	Lobar pneumonia; chronic bronchitis.				Not abundant.	Irregular; not circumscribed.	Absent.	Mixed; small cells more abundant in medulla.	Very abundant; dense hyaline fibrous tissue and fat; invasion of lobules; few granular oxyphilic cells.	Moderately numerous pycnotic cells with nuclear extrusions.	No degenerative changes; no phagocytosis.	Very numerous large sequestra, with beginning calcification.	Marked sclerosis.	Advanced "accidental" involution.
Do.....	M.	6 months.	Otitis media, suppurative; no other lesions.	+++	40 grams.	Sudden death.	Very abundant.	Closely apposed; circumscribed.	Distinct.	Cortex, small cells; medulla, mixed; marginal zone indistinct.	Thin fibrous septa; oxyphilic cells numerous, both within lobule and in septa.	In places nuclear extrusions and fragmentation.	No degenerative changes, no phagocytosis.	Small cell complexes; few small necrotic forms and cysts.	Normal.	Normal gland. Probably idiopathic "status" death.
218.....	F.	22 years.	Acute infective endocarditis, multiple emboli, etc.; healed pulmonary tuberculosis.	+	Large (?).	2 weeks (?).	Abundant.	Irregular; poorly circumscribed; cortex follicular in places.	Indistinct; rarefaction of cortex.	Reticular.	Abundant; fat and hyaline fibrous tissue; no granular oxyphilic cells; mast cells numerous in septa and within lobules; occasional plasma cells.	Moderate pycnosis and fragmentation.	In cortical follicles reticular cells show vacuolar degeneration and phagocytosis.	Small cell complexes and necrotic forms.	Swelling and proliferation of endothelium; hyaline degeneration of capillary walls.	Acute degeneration upon chronic involutional changes.
1872.....	M.	6 hours.	Hemorrhagic bronchopneumonia; tallipes equinus.	0	—	—	Abundant.	Regular; circumscribed.	Absent; marked rarefaction of cortex.	Reticular; small cells more numerous in medulla.	Very abundant; loose fibrous tissue; very numerous mononuclear cells with oxyphilic granule; also occasional polynuclear eosinophiles.	Slight pycnosis; no fragmentation.	No degenerative changes.	Numerous hypertrophic cell complexes and necrotic Hassall bodies.	Slight sclerosis.	Congenital involutional changes.
1977.....	M.	15 years.	Suppurative otitis media and meningitis (streptococcus).	+	10.5 grams.	12 days.	Fairly abundant.	Very irregular; poorly circumscribed.	Absent.	Reticular cells.	Abundant; in places invading lobules; no oxyphilic cells; no mast cells.	Marked pycnosis and fragmentation.	Marked degeneration, many isolated ovoid vacuolated reticular cells; moderate phagocytosis.	Numerous cell complexes and small necrotic forms; no large sequestra.	Slight hyaline degeneration; marked proliferation of adventitia.	Advanced acute degeneration, with beginning fibrosis.

r Epithelium.	Hassall Bodies.	Blood Vessels.	Remarks.
of reticular cells ins deeply with cute degenerative	Numerous very large necrotic forms; no cell complexes or "young" forms	Marked adventitial thickening.	Advanced "accidental" involution.
tive changes; dle-shaped cells; tosis.	Numerous cell complexes; small necrotic forms; some calcareous.	Marked adventitial thickening.	Advanced "accidental" involution; no acute changes.
ny reticular cells ed vacuolar de-	Numerous small necrotic and calcareous forms.	Capillaries show hyaline degeneration; larger vessels show adventitial thickening.	Extreme sclerosis and atrophy, with foci of acute degeneration.
eneration; mod- cytosis.	Many cell complexes and unformed Hassall bodies.	Slight thickening of adventitia.	Acute degeneration.
vacuolar degen- rtex composed legenerated retic-	Very numerous small cell complexes and Hassall bodies with necrotic centers and calcification.	Proliferation of adventitia; capillaries numerous and congested.	Marked atrophy; rarefaction of cortex; vacuolar degeneration of reticulum; replacement fibrosis.
arked vacuolar n and phagocy-	Numerous small necrotic and calcareous forms.	Marked sclerosis.	Chronic involution and acute degeneration.
ted cells found; ocytosis.	Not numerous, small necrotic and calcareous forms.	Slight perivascular thickening.	

Name or Acc. No.	Sex.	Age.	Anatomical Diagnosis.	Status Lymph.	Weight of Thymus.	Duration of Illness.	Amount of Thymic Tissue.	Shape of Lobules.	Differentiation of Cortex and Medulla.	Predominant Cell Type.	Interstitium.	Small Thymus Cells.	Reticular Epithelium.	Hassall Bodies.	Blood Vessels.	Remarks.
2031.....	M.	15 years.	Chronic interstitial nephritis.	+	11.5 grams.	Long.	Moderate.	Irregular; not circumscribed.	Absent.		Abundant, fibrous, marked invasion of lobules.	Moderate pycnosis; no fragmentation.	Protoplasm of reticular cells dense; stains deeply with eosin; no acute degenerative changes.	Numerous very large necrotic forms, no cell complexes or "young" forms.	Marked adventitial thickening.	Advanced "accidental" involution.
2035.....	F.	17 years.	Congenital idiocy; chronic interstitial nephritis.	0	9.5 grams.	—	Moderate.	Irregular; poorly circumscribed.	Absent.	Mixed.	Abundant; dense fibrous tissue, no fat; slight intralobular sclerosis; no oxyphilic cells.	Slight pycnosis; most cells well preserved; no nuclear extrusions.	No degenerative changes; many spindle-shaped cells; no phagocytosis.	Numerous cell complexes, small necrotic forms; some calcareous.	Marked adventitial thickening.	Advanced "accidental" involution; no acute changes.
2085.....	M.	1 year.	Congenital diplegia.	0	3.5 grams.	Life.	Scant.	Irregular; not circumscribed.	Absent.	Spindle-shaped reticular cells.	Very abundant, hyaline connective tissue, marked intralobular sclerosis; no granular oxyphilic cells	Marked pycnosis and fragmentation	In places many reticular cells show marked vacuolar degeneration	Numerous small necrotic and calcareous forms.	Capillaries show hyaline degeneration; larger vessels show adventitial thickening.	Extreme sclerosis and atrophy, with foci of acute degeneration.
2093.....	M.	9 days.	Congenital internal hydrocephalus, prematurity.			Life.	Abundant.	Regular; circumscribed; closely apposed.	Absent.	Mixed, many transitional cell forms.	Somewhat increased in amount; no invasion of lobules, groups of oxyphilic cells in stroma.	Marked pycnosis and fragmentation.	Vacuolar degeneration; moderate phagocytosis.	Many cell complexes and unformed Hassall bodies.	Slight thickening of adventitia.	Acute degeneration.
2090.....	M.	2 months.	Marasmus; suppurative otitis media.	0	2.5 grams.	Life.	Relatively not abundant.	Irregular in places, not circumscribed.	Absent.	Reticular elements predominate in cortex; medulla, mixed.	Dense fibrous septa; no fat, slight invasion of lobules, no granular oxyphilic cells; few mast cells.	Few pycnotic and fragmented forms; nuclear extrusions rarely seen.	Very marked vacuolar degeneration; cortex composed largely of degenerated reticular cells.	Very numerous small cell complexes and Hassall bodies with necrotic centers and calcification.	Proliferation of adventitia; capillaries numerous and congested.	Marked atrophy; rarefaction of cortex; vacuolar degeneration of reticulum; replacement fibrosis.
1897.....	M.	15 years.	Juvenile paresis.	++	14.5 grams.	1 year.	Moderate.	Irregular; not well circumscribed; fatty invasion of lobules.	Absent.	Mixed; rarefaction of cortex.	Very abundant; chiefly fatty; numerous oxyphilic cells within lobules and in septa.	In general, well preserved; few pycnotic cells.	In places marked vacuolar degeneration and phagocytosis.	Numerous small necrotic and calcareous forms.	Marked sclerosis.	Chronic involution and acute degeneration.
N.Y. Hosp.	M.	37 years.	Chronic valvular disease, tuberculous lymphadenitis.	+++	110 grams.	3 years.	Very abundant.	Regular; circumscribed; closely apposed.	Not distinct.	Small cells, closely aggregated.	Scant; fibrous septa with small groups of fat cells; no oxyphilic cells; few mast cells.	Very slight pycnosis; no nuclear extrusions.	Few vacuolated cells found, slight phagocytosis.	Not numerous, small necrotic and calcareous forms.	Slight perivascular thickening.	

In attempting to draw general conclusions from such observations one encounters numerous difficulties. There are many variable factors in each case: the particular stage of evolution or involution of the gland at the onset of the disease; the modifying influence of previous illnesses upon its structure; the effect of the associated Status lymphaticus; the general nutrition of the subject, and so on. Certain broad facts, however, stand out clearly enough. The small cells appear to be especially sensitive to toxic influences of all sorts, and very early in the course of acute infections undergo extensive disintegration. This is manifested by a loss of the nuclear structure, pycnosis, irregularity of the nuclear outline, fragmentation and, finally, solution of the nuclear fragments. In the course of this karyolytic degenerative process the nuclei may assume very bizarre forms, differing decidedly from the radial extrusion of nuclear particles which we have ventured to correlate with the specific secretory activity of the small thymus cells. The extent of these necrobiotic changes depends apparently upon the nature and severity of the infection, and appears to be most pronounced during the early stage of the illness.

The rarefaction of the cortex, where the small cells are most closely aggregated, is undoubtedly due to this extensive destruction of the small cells. This may be so extreme that the normal differentiation is entirely obscured. It is not only in the cortex, however, that the small cells go to pieces, but in the medullary portions as well. In some cases the destruction of the small cells appears to be limited to certain areas only, in others it is more uniformly distributed. The effect of the rarefaction of the cortical cells is to render the marginal zone more distinct.

The reticular cells also undergo very characteristic changes. They appear to lose their protoplasmic connections with the neighboring cells and take on an oval form. The cytoplasm frequently shows an exquisite vacuolation. Whether this indicates a fatty degeneration I am not prepared to say. In one case, however, in which the material was fixed in Fleming's solution, many of the exfoliated reticular cells were filled with black staining globules. We have already referred to the phagocytic power which these reticular cells possess. In certain cases they are found closely packed with small round pycnotic nuclei, each surrounded by a narrow halo; I have counted as many as twenty in a single cell. In other cases phagocytosis is less marked, and one has to search many fields before finding a phagocytic cell.

With the disintegration of the cytoplasm of the reticular cells the nuclei become hydropic, stain palely, and the nucleolus often takes a distinct oxyphilic stain. The cytoplasm becomes ragged and the cell eventually goes to pieces.

It will be seen by referring to the tables that phagocytosis is most pronounced in the severe infections of short duration—notably in the cases of epidemic cerebrospinal meingitis dying within three or four days. It was also extremely marked in the case of a child 3½ years old, who died after thirty-six hours of exposure and starvation.

Although the extensive fragmentation of the small thymic cells and the vacuolar degeneration of the reticular epithelium is characteristic of acute degenerative conditions, the same process occurs on a less extended scale in the chronic atrophy of the gland. Thus in a child of 1 year, with congenital diplegia (Case 2085) and marked wasting, the sclerotic thymus weighing only 3.5 grams showed many fairly circumscribed areas in the parenchyma where the fragmentation of the small cells and the vacuolar degeneration of the reticular cells were much in evidence. Many phagocytic cells were present in these areas.

Following the destruction of the parenchymal cells there ensues a proliferation of the connective tissue fibrils, leading in advanced cases to a marked sclerosis of the gland. Hammar states that even in extreme accidental involution there is no increase in the absolute amount of fibrous tissue present; this assertion is based upon the employment of the wax-plate method, which is obviously inapplicable to a determination of the new-formed tissue within the lobules. My sections of atrophic glands demonstrate conclusively a relative increase in the connective tissue, not only in the septa but within the lobules as well. The new connective tissue fibrils take their origin from the adventitia of the intralobular capillaries and traverse the parenchymal substance in all directions. This is beautifully brought out in sections stained with Mallory's aniline blue or Bielschowsky's silver method. There is also an ingrowth of fibrous tissue from the periphery of the lobules so that the limiting membrane is disorganized and the lobular outline is rendered indistinct. This extensive invasion of the cortical cells by new-formed connective tissue fibers has probably led Hammar to the statement that there is a true emigration of "lymphoid" cells into the interstitium. I have never seen small cells in such a situation as to suggest that they were in the act of penetrating the intact basement membrane upon which the marginal zone of reticular cells rests. It is true that groups of lymphoid

and plasma cells are not infrequently found in the stroma in the neighborhood of the smaller blood vessels. There seems to me, however, to be no reason for believing that these are small thymus cells which have emigrated from within the confines of the lobules, and I am more inclined to consider them as indicating chronic inflammatory changes.

It is difficult to decide positively whether the fibrosis of the thymus represents merely a replacement process, or whether there may occur at times a true primary sclerosis of the gland. In the atrophic involuted organ the reticular cells may, through compression, take on an elongated spindle-shaped form and thus bear a certain resemblance to young connective tissue cells. Without special differential stains it may be impossible to distinguish these from fibro-blasts. Where the margin of the lobule is destroyed the appearance suggests, and has not infrequently been mistaken for, actively-growing connective tissue and endothelium. In the light of our recent knowledge such misintepretation should no longer occur. In the material which I have studied I have not seen a true proliferation of the connective tissue cells either in the septa or within the lobules; on the other hand, the connective tissue fibrils become more numerous, and in later stages undergo hyaline degeneration. In several cases there was noted a pronounced thickening of the adventitia of the larger blood vessels.

The differences between the "accidental" and the normal involution of the thymus have been pointed out by Hammar, and in the main our study supports his view. It seems to me that the essential difference in the appearance of the organ is due to the fact that whereas normally the destruction of the thymic elements proceeds slowly and uniformly and the general structure of the lobules is not disturbed, under pathological conditions the destruction of the parenchymal cells is more rapid, more intense, and less evenly distributed. The thinning out of the cortex and the subsequent loss of the normal contours of the lobules, the replacement hyperplasia of the connective tissue in the septa and about the intralobular blood vessels are the distinguishing characters of the "accidental" involution of the organ.

How far a regeneration of the thymic elements may occur after the acute degeneration associated with infectious diseases is, of course, entirely unknown. In fact, the entire subject of regeneration in the thymus demands further study, and might profitably be attacked along experimental lines.

VII. General Conclusions.

The thymus gland is an epithelial organ composed of two types of epithelial cells. The first, designated by the term "reticular epithelium," serves as a supporting structure, has the power of building fibrils, and is actively phagocytic towards the small cells of the second type. The Hassall bodies are formed by cell-complexes of hypertrophic reticular cells; new Hassall bodies are developed throughout the growth period of the gland, the fully developed forms undergoing necrosis and calcification. It is probable, also, although the writer is unwilling to express himself positively upon this point, that the reticular cells may become differentiated into small cells when a renewal of growth takes place in adult life. The small thymic cells are also epithelial in origin and nature and are not lymphocytes. The thymus histogenetically and histologically bears no relation to the lymph glands.

The thymus gland is in a state of evolution until the age of puberty. It then undergoes regressive changes, at first abruptly, later more gradually. It is, in all probability, a functional organ throughout life.

There is a rapid reduction in the weight of the thymus in acute disease, due to a destruction of the thymic epithelium. In chronic diseases this is accompanied by a replacement hyperplasia of the connective tissue. There are no distinctive histological features in the thymus of individuals showing the lymphatic state, or in individuals showing this constitution and dying suddenly from unknown causes. Normal involution is, however, delayed in subjects manifesting the lymphatic state.

In concluding, I wish to express my grateful indebtedness to Dr. Otto H. Schultze, who supplied me with complete series of early rabbit and human embryos, as well as much human material obtained from his service as Coroner's Physician. I wish also to thank Dr. Charles Norris, Director of the Laboratory, for his unfailing assistance and encouragement. The photographs were taken by Dr. Jaches of the Loomis Laboratory, Cornell University Medical School.

Note—Since the above article has gone to press Maximow has published an important paper (Archiv. f. Mikr. Anat., Bd. 74, Heft. 3, October 28, 1909), sustaining the view that the small thymus cells arise from mesenchymal elements, which invade the gland at an early stage of fetal development and become differentiated into true lymphocytes. The writer regrets that he is unable to include a critical review of Maximow's work.

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THE BACTERIOLOGY OF THE BLOOD IN CONVALESCENCE FROM TYPHOID FEVER.*

WITH A THEORY OF THE PATHOGENESIS OF THE DISEASE.

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The discovery of the constant presence of the typhoid bacillus in the blood of patients suffering from typhoid fever made it probable that the symptoms of the disease were dependent, in part at least, upon the destruction of bacilli in the blood. The exact relation of the bacilliemia to the course of the disease was not, however, disclosed by this discovery. Subsequent studies of the blood in man and experiments upon lower animals with regard to the relative destruction of bacilli in the blood and in other parts of the body have furnished the basis for a more detailed account of the part played by the bacilliemia in the evolution of the disease.

In 1907 we advanced the following theory of the pathogenesis of typhoid fever: That the bacillus first finds its way from the alimentary tract to the lymph nodes and spleen, where it develops chiefly and whence it invades the blood stream. It is doubtful whether the bacillus multiplies in the blood; its presence there in all probability simply represents an overflow from the lymphoid organs. That the symptoms of the disease are caused by the destruction of vast numbers of bacilli in the blood with liberation of their endotoxins, and the consequent reaction on the part of the host. When the endotoxins are liberated elsewhere in the body, *e.g.*, in abscesses, the symptomatology is not that of typhoid fever. There seems to be a definite relation in the evolution of typhoid fever between the bacillemia and the symptoms. The duration of the febrile movement is measured by the persistence of the bacillemia (fever attending complications is not included in this statement).

With the object of testing further the truth of this hypothesis, we have continued the study of the bacteriology of the blood into the convalescence of typhoid fever. But before giving the results of our own work it will be desirable to review that of others.

Prior to the year 1906 all investigators except Conradi were agreed that the bacillus disappeared from the blood at or about the time of defervescence. Conradi recovered the bacillus from the blood of two cases after they had defervesced and drew the conclusion that the bacillemia persisted into convalescence.

Epstein reported in 1908 that a number of his cases yielded positive results shortly before defervescence, that is, one, two or three days, but in no case was a positive result obtained after defervescence was established.

During the year 1907 three papers appeared on the bacteriology of the blood in convalescence from typhoid fever. Gennari, using Conradi's bile method, recovered the bacillus from the blood eight times, at periods varying from the second to the fourteenth day (he does not state how many cases were examined).

Meyer, using Castellani's method, recovered the bacillus from the blood up to the eighth week of convalescence (he likewise does not state how many cases were examined).

Gildemeister reported one case in which he had found the bacillus after defervescense.

In 1908, likewise, several papers were published. Lesieur recovered the bacillus from the blood in six of thirty-three cases; the patients had been fever-free for periods varying from four to six weeks.

Stühlern, in a study of thirty-three cases, found the bacillus once, five days after defervescence.

Lüdke's paper was published in January of this year. He examined the blood of eight cases after defervescence. In six of them the result was negative. In one case he found the bacillus on the first afebrile day—one colony on five plates, and in the other, on the second afebrile day—two colonies on three plates.

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The Bellevue Hospital Cases—There are forty-six cases with one hundred and ten examinations in the present series. We employed Conrad's bile method in all of them and the usual technic in drawing the blood. After having examined a few cases in the last days of the primary fever and a few more in the first afebrile period, we decided that complete examinations of each case would furnish better standards of comparison. Accordingly, in the remaining cases we examined the blood at the height of the disease, on different days of convalescence, during relapses, when they occurred, and in the subsequent afebrile period. Though our principal object was the study of the blood in convalescence, a number of suggestive observations were made in other stages of the disease.

The cases may be divided into four groups: 1, examined only toward the end of the first febrile period; 2, examined only in the first afebrile period; 3, examined in both the first febrile and first afebrile periods; 4, with relapses.

TABLE I.

First Febrile Period.

No.	Day.	Bacillus.	Remarks.
1	8, 10, 28	+ + —	
2	19, 20, 24	— — —	
3	20	—	
4	15	—	
5	11	—	

TABLE II.

First Afebrile Period.

No.	Day.	Bacillus.	Remarks.
1	18	—	
2	25	—	
3	14	—	
4	18	—	
5	10	—	
6	4	—	

TABLE III.

Febrile and First Afebrile Periods.

No.	Febrile.		Afebrile.		Remarks.
	Day.	Bacillus.	Day.	Bacillus.	
1	11	+	1	—	
2	8	+	3	—	
3	14	+	6	—	
4	6	+	3	—	
5	10	+	6, 13	— —	
6	14	+	2, 7, 15	+ — —	
7	7	+	5	—	
8	7	+	1	—	
9	16	+	1	—	
10	8	+	4	—	
11	4	+	9	—	
12	7	+	10	—	
13	5	+	13	—	
14	13	+	9	—	
15	7	+	8	—	
16	11	+	5	—	
17	7, 12, 17	— — +	3, 7	— —	
18	16	+	3, 13	— —	
19	29	+	22	—	
20	15	+	9	—	
21	27	+	7	—	
22	15	+	4	—	
23	9	+	4, 8	— —	
24	10	+	1	—	
25	12	—	5	—	
26	7	—	3, 8	— —	10-day Fever.

TABLE IV.

Cases with Relapses.

No.	Febrile.		Afebrile.		Relapse.		Afebrile.		Remarks.
	Day.	Bacillus.	Day.	Bacillus.	Day.	Bacillus.	Day.	Bacillus.	
1.....	....	....	3	—	5	+	4	—	
2.....	....	....	1, 7	— —	13	—	3	—	
3.....	7	—	5	—	3	+	6	—	
4.....	20	+	....	....	9, 13	+ +	17	—	
5.....	10	+	7	—	4	+	18	—	
6.....	8	—	2	—	4	—	3	—	
7.....	9	+	....	....	1	+	5	—	
8.....	15, 21, 27	— — —	....	....	6	+	3	—	
9.....	....	....	....	....	4	+	2, 7	— —	

There are five cases in the first group with nine examinations. The group, though small, illustrated the diminishing bacillemia, and the uncertainty of recovering the bacillus, in the last days of the fever. Three examinations were made in Case 2, when the temperature was intermittent, and all were negative. Case 5 was of the short-duration variety. Cases 25 and 26, Table III., also of the short-duration variety, may be mentioned here.

The cases examined in the afebrile period (Tables II., III., IV.) were forty-one in number with fifty-six examinations, made from the first to the twenty-fifth day of convalescence. The results were negative in all but one case (No. 6, Table III.), in which the bacillus was recovered on the second afebrile day.

Case 13, Table III., gave a negative result during a recrudescence of the fever.

Case 17, Table III., and Cases 3 and 8, Table IV., demonstrate that even several negative examinations of the blood made at the height of the disease cannot be considered to preclude the diagnosis of typhoid fever, as stated by Schottmueller and later by Libman. In Case 17 examinations made on the seventh and twelfth days of the disease were negative, while another examination on the seventeenth day was positive. In Cases 3 and 8 the bacillus was not found until the relapse.

In Case 7, Table IV., the bacillus was found on the first day of the relapse, in fact before it was realized that a relapse had set in.

In Case 6, Table IV., examinations made in the primary attack, in the first afebrile period, in the relapse, and in the second afebrile period were all negative.

Discussion of the Results—While prior to 1906 no studies of the blood in convalescence had been undertaken, some cases had been examined in the last days of the fever and a smaller number after defervescence, and the opinion prevailed that the bacillemia disappeared at or about the time convalescence began. Our own results in this and in former series of cases support this view. But the positive results which have since been obtained during convalescence, though not numerous, cannot be ignored and an attempt must be made to reconcile the discrepancies.

It is admitted by all who have studied the subject that typhoid fever is characterized by a bacillemia which is most easily demonstrated in the earlier periods of the disease and thereafter progressively diminishes. Our belief is that the febrile movement and the bacillemia are conterminous. But it cannot be assumed that the bacilli disappear from the body, even though they disappear from the blood, at the beginning of convalescence.

Lüdke found after intravenous injections in guinea-pigs and rabbits that typhoid bacilli could be grown from the spleen and, with less certainty, from the bone-marrow, up to the beginning of the third week. Buxton found in his experiments on the absorption of typhoid bacilli from the peritoneal cavity that the bacilli were often still present in large numbers in the lymph nodes (especially the anterior mediastinal) and spleen after they had entirely disappeared from the blood and almost entirely from the liver, lung, and bone-marrow.

We find that in discussions on this subject the bone-marrow is always included in the lymphatic system, and is supposed to harbor the bacilli in the same way as the spleen and lymph nodes, but Buxton's experiments with rabbits have not shown that the bacilli persist in the bone-marrow longer than in the liver, lung, or kidney. Our impression is that the lymphocyte-producing organs are essentially those which harbor the bacilli, but not the leucocyte-producing organs, such as the bone-marrow.

While we know of no studies which have been made upon man, there is evidence that the bacilli remain latent in the body for undetermined periods (we do not include in this statement bacillus carriers who harbor the bacillus in the gall bladder, biliary passages, intestine, or urinary bladder). For example, relapses have occurred as long as fifty-seven days after defervescence (Curschmann) and post-typhoid sup-

purative bone lesions have been known to occur as late as two years after the primary attack (Dudgeon and Gray). So far as our present knowledge goes, these conditions are not due to auto-infection in carriers (though Levy and Kayser have reported a case which they believe to have been such) or to re-infection from without. It is much more probable that they are caused by bacilli which have remained latent in the body. The continued enlargement of the spleen, seen in many cases which relapse, at least suggests that the growth of bacilli has not been completely checked. If latency is admitted, it is not unlikely that small numbers of bacilli may find their way to the blood, especially in the earlier days of convalescence, and be recovered in cultures. In this way the discrepancies in the results of different investigators may be reconciled. But apparently positive results are dependent upon the fortuitous drawing of blood containing bacilli.

Theory that the Endotoxins are Liberated Chiefly in the Blood—The symptoms of typhoid fever undoubtedly represent the reaction of the host to endotoxins which have been liberated in the body by the destruction of bacilli. Experimentally Buxton found that destruction occurred most rapidly in the blood and confirmed Bail's belief that, once the bacilli reached the organs, they found an environment which protected them to a great extent from the bactericidal action of the blood.

While it has not yet been decided to what relative extent in man destruction occurs in the blood and in other parts of the body, the following facts lead to the belief that the blood is the chief agent of destruction in man as in the lower animals; the correspondence in time of the bacillemia and the symptoms, and the negative results of cultures made at the height of the disease in some severe cases. The sudden occurrence of a relapse, with a return of the bacillemia, also supports the theory, for if destruction of bacilli was actively carried on in the lymph nodes and the spleen, where the bacilli remain after the temperature ceases, the liberation of endotoxins should give rise to symptoms. The alternative to this view is the theory that as the disease advances the bacilli lose in virulence and become saprophytic. Jürgens and Lüdke, on the other hand, both state that they recovered bacilli from the blood during relapses which were more virulent than those obtained during the primary attack. It must be added, however, that the determination of the virulence of the typhoid bacillus is so difficult and uncertain that many bacteriologists refuse to accept the results of such experiments.

Epstein has raised the point whether the bacillemia precedes, or corresponds with, the symptoms. Conradi found the bacillus in the blood of a child four days before the onset of symptoms, but, as in the cases where the bacillus has been found after defervescence, it may reasonably be argued that this does not represent the rule. At least, until the constant presence of the bacillus in the blood before the development of symptoms is established, such a theory cannot be maintained. Such facts as we possess indicate that the bacillemia and the symptoms correspond in time; the bacillus is not usually found except during the febrile movement: the abrupt onset of some cases, and the abrupt onset of relapses with a return of the bacillemia (we have recovered the bacillus on the first day of the relapse) indicate that the bacilli are suddenly discharged into the blood about the time the symptoms begin.

The theory that the blood is the chief agent of destruction, if true, would also explain some results of blood examinations which at present seem paradoxical: one of these is the lack of correspondence between the number of bacilli in the blood and the severity of the disease, a fact which has been noted by most investigators. In explanation it may be supposed that the bacilli have been rapidly killed off and that the blood drawn contains none that are viable. On the other hand, the uncertainty of the result of blood examinations in short-duration cases, and the mild character of the symptoms, are probably due to the relatively small numbers of bacilli in the blood. This theory will also explain the belated growth of bacilli on artificial media which is seen in some cases—bacilli which are nearly lifeless when drawn become viable on being removed from the unfavorable influence of the blood. It will also explain the negative results which were the rule before the methods of growing the bacillus from the blood were perfected.

Summary—With the additional facts which this study has placed at our disposal, we would suggest the following elaboration of our original theory: That the atrium of infection is the lymphatic structures of the intestinal wall. Thence the bacilli invade the general lymphatic system and spleen where they grow chiefly and where relatively few bacilli are destroyed. A limited number of bacilli may filter through into the blood during the incubation period of the disease. When the development of the bacilli has reached a certain grade, they overflow in quantity into the blood, where they are destroyed and their endotoxins set free, and the symptoms

represent the reaction on the part of the host. As the disease advances, if the patient is making a successful fight, the growth of the bacilli in the organs is gradually brought under control by the immunity processes, fewer bacilli are discharged into the blood, and the symptoms lessen in severity. In fatal cases, when death is not due to an accident, as hemorrhage, the growth of bacilli in the organs proceeds unchecked and the symptoms remain of the same, or take on increased, intensity.

At or about the time of defervescence the bacilli practically disappear from the blood. Though a few may filter through into the blood, the symptoms come to an end and convalescence proceeds normally. In cases in which an intermittent temperature, which is not due to a complication, continues after the original febrile movement is at an end, it is not unlikely that the growth of bacilli in the organs has not been completely checked and that a limited number continue to be discharged into the blood. In some cases of typhoid fever the spleen remains enlarged after defervescence and later a relapse occurs. This enlargement suggests that though the growth of bacilli both here and in the lymph nodes has temporarily been brought under control, complete immunity has not been established, and later, through agencies which are still unknown, rapid multiplication occurs, the bacilli are discharged into the blood, are destroyed, and the symptoms of the relapse become manifest.

The late development of local suppurative processes, due to the typhoid bacillus, seems to indicate that recovery from an attack of typhoid fever does not confer local immunity to the bacillus.

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SURGICAL ASPECT OF TYPHOID FEVER.*

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A tabulation of the surgical complications and sequelæ of typhoid fever, would include lesions of almost every organ of the body. There occur phlebitis, thrombosis and embolism; gangrene, either localized or of the extremities; hæmatoma in the muscles, especially of the abdominal wall; abscesses of the skin, subcutaneous tissue, spleen, liver, mesenteric glands, kidneys, brain, thyroid, parotid, testicle, breast, and even of the heart muscle; chondritis and perichondritis, especially of the larynx; inflammation of the bones and joints; suppurative pericarditis and empyema; cholecystitis and appendicitis, with or without perforation, and perforation of the intestine. As the diagnosis and treatment of most of those conditions presents no material difference, whether or not they occur as a complication of typhoid fever, only those showing characteristics due to this etiological factor, will be briefly considered in this paper.

Thus the treatment of phlebitis, gangrene, or abscesses wherever occurring, empyema, mastitis, otitis media, etc., is based on the same general surgical principles as when the cause is other than the bacillus of Eberth alone, or associated with some other pyogenic organism.

Joint inflammation complicating typhoid calls for brief consideration. The lesion may be due to either infection with the bacillus typhosis alone or to mixed infection. True typhoidal arthritis rarely goes on to suppuration or results in ankylosis. The

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hip-joint is most frequently involved, and there is a marked tendency to spontaneous dislocation, especially in young patients. Less commonly occurs rheumatic or septic arthritis as a complication of typhoid fever. The typhoid spine belongs within the realm of the orthopædic surgeon.

Bone lesions should be classified among the sequelæ, rather than the complications of typhoid, as they frequently occur weeks or months after the fever. They are comparatively common. Either the typhoid bacillus in pure culture or a mixed infection may be found. The tibia is most often affected, the ribs next most frequently. Multiple lesions are not uncommon. Periostitis is the most frequent, but any inflammatory lesion of the bone may occur. There is usually little elevation of the temperature caused by bone inflammation due to the bacillus typhosis alone. Traumatism and muscular strain are the exciting causes of periosteal and bone lesions and therefore to be guarded against during the course of the fever, and in convalescence.

Laryngeal complications, acute oedema, ulceration, chondritis and perichondritis are not rare, and when present often call for such urgent treatment that they may be briefly alluded to here. Ulcer of the larynx is said to be present in ten to eighteen per cent. of the cases, although it is infrequently diagnosed. Two hundred and eighty-one cases of laryngeal complications have been collected from the literature by Reiser (1). In two hundred and forty-three cases, there was a mortality of sixty-five per cent. Symptoms appear usually late in the course of the fever or during convalescence. Hoarseness or aphonia, dysphagia, dyspnœa or inspiratory stridor call attention to the probability of a laryngeal lesion, and preparations for tracheotomy should be made at once, as serious symptoms develop with great suddenness, and the patient may choke to death unless the physician is prepared for this complication.

The most frequent and fatal complication of typhoid fever is certainly perforation. It has been estimated that five hundred thousand cases of typhoid occur annually in the United States, Taylor (2). That the mortality is ten per cent. That thirty per cent. of the mortality is due to perforation, Osler (3). That two and a half to three per cent. of the total cases, that is fifteen to sixteen thousand, Long (4), twenty-five thousand, Woolsey (5), die annually in the United States as a result of perforation. Patterson (6) has collected twenty-one thousand and two hundred and fifteen cases of typhoid, with six hundred and seventy-one perforations, three and sixteen hundredths per cent. The mortality without operation is practically one hundred per cent. In three hundred and sixty-nine operations collected by Patterson, there were two hundred and forty-two deaths, a mortality of sixty-five and fifty-eight hundredths per cent. These added to three hundred and sixty-two cases with two hundred and sixty-eight deaths, a mortality of seventy-four and three hundredths per cent. previously reported by Harte and Ashhurst (7), gives a total mortality in seven hundred and thirty-one cases of sixty-nine and eight-tenths per cent. In Patterson's series, sixty-eight operations were on children, with a mortality of forty-five and fifty-eight hundredths per cent. Thus, by examination of the foregoing, while it is granted that operative statistics made up from reported cases are always unduly favorable, it would seem fair to estimate that at least between four thousand and five thousand lives might be saved annually in the United States alone, by surgical procedure.

Perforations may occur at any time after the first week, during the course of the fever, in a relapse or convalescence. It is most frequent during the third week, fifty-six and six-tenths per cent. occurring during the second and third week (Harte and Ashhurst), seventy per cent. between the second and fifth week (Patterson). The most frequent site of perforation is within twelve inches if the ileocæcal valve, seventy-three per cent. (Harte and Ashhurst). Ninety-five per cent. of all perforations occur in the last three feet of the ileum, Haggard (8). Perforations of the appendix, colon, cæcum, Meckel's diverticulum, rectum, jejunum and stomach also occur. The perforation is usually found on that part of the intestine opposite the mesenteric attachment, and was single in eighty-five and one-half per cent. of the total seven hundred and thirty-one cases reported. Adhesions are rarely found except in cases with mixed infection. This complication is more frequent in males, in the proportion of four to one.

While perforation occurs in mild or ambulatory cases, it appears to be more frequent in severe cases where there is deep ulceration. Distention, improper diet, increased peristalsis, abdominal straining, are mentioned as etiological factors.

The first, and as a rule, the most reliable and constant symptom of perforation is sharp *pain,* usually in the lower right quadrant of the abdomen. *Tenderness* in the same region is present at the same time, and if no operation is performed, spreads as the peritoneal irritation increases. The degree of these two symptoms may be difficult to determine in a very sick patient in the so-called typhoid state. *Rigidity,*

as a rule, appears early. It is not a sign of perforation, but of peritoneal irritation. It should not be waited for before operation, but when present, is a definite indication for operation. *Loss of,* or diminished *liver dullness,* is a valuable sign. It depends on the size of the perforation, and the amount of gas escaping. In the presence of considerable distention, it may be hard to determine. When present with a flat abdomen it is a pathognomonic.

A sudden rise in the pulse rate is strong corroborative evidence, in the presence of other symptoms, of perforation or the absence of signs, of hemorrhage. It was formerly stated that a fall of temperature always accompanied a perforation. This is not so. In the seventeen cases occurring at the Presbyterian Hospital, analyzed by Woolsey, in no case was a fall observed. This agrees with the experience of others. An *elevation* of the *temperature* usually accompanies the increased pulse and respiratory rate, and is the rule, but a drop in the temperature does sometimes occur, as the writer has seen a fall from one hundred and three degrees Fahrenheit to ninety-eight and six-tenths degrees Fahrenheit in a few hours, following a perforation. *Vomiting* occurs in a number of cases, but is not constant, and may be due to so many other causes, that it is not of great value in determining the diagnosis.

The *leucocyte count* is said to be of little value. Unquestionably this is so, if only a single count be made. Certainly, it is not of sufficient value to defer operation while repeated counts are made. But if because of doubts or other reasons, operation is postponed, it is usual to find some increase in the total leucocytes and a proportionately polynuclear increase. In a case operated on by the writer at Bellevue Hospital within the last three weeks, a count made at eleven p. m. on September twenty-fifth, an hour and a half after the patient first began to have pain, showed four thousand five hundred leucocytes, with fifty-six per cent. polynuclear cells. Three hours later, while on the operating table just before operation was begun, examination showed thirteen thousand leucocytes with seventy-eight per cent. polynuclears. In a girl 15 years of age, admitted to St. Luke's Hospital forty-eight hours after perforation, the count showed twenty-six thousand leucocytes, with eighty-three per cent. polynuclears. Certainly, one should not wait for such a condition to develop. In another case in St. Luke's Hospital, the count rose from three thousand eight hundred with sixty per cent., to four thousand eight hundred with seventy-six per cent., eleven hours after perforation.

Movable, increasing *dullness in the flanks,* most marked on the right side, is a symptom due to considerable escape of intestinal contents or fluid exuded by the peritoneum, due to irritation, and is also a late symptom. While corroborative, it should not be waited for.

A change in the facial expression, called by the French "abattement," or weakening of the countenance, can sometimes be observed, especially by the physician in charge of the patient. This differs from, and precedes the characteristic "abdominal facies" of general peritonitis, which appears later unless operation is performed.

It is important to remember that all of these signs should be sought, but not waited for. The most reliable early symptoms are sudden, constant and severe pain, tenderness, and increased pulse rate. These are often sufficient to indicate operation. With rigidity or diminished liver dullness (distention being absent), or both in addition, operation is imperative. The other symptoms are corroborative.

The success of an operation depends largely on its early performance, although a successful case has been reported by Moskowitz (9), operated on three and a half days after the apparent time of perforation. The operation can be done under local anæsthesia, but general anæsthesia with ether is preferable. The incision should be made through the lower part of the right rectus muscle, the cæcum sought for, and the small intestine examined, beginning at the ileocæcal valve. The perforation is best closed by Lembert sutures, the first layer of Pagenstecher celluloid-linen thread, the second layer of double nought chromic catgut. The writer has found the purse-string suture unsatisfactory on account of the indurated area forming the base of the ulcer, and surrounding the perforation. Where possible the omentum should be brought down to cover the sutured area. No attempt should be made to excise the ulcer. If there has been much soiling of the peritoneum by the escape of intestinal contents or an extensive suppurative peritonitis is present, copious saline irrigation should be employed, otherwise not, and only gentle sponging be made use of. Drainage should be obtained by folded rubber dental dam, which is superior to gauze or tube drainage. One piece should go down into the pelvis, the other to the sutured intestine. The after treatment is that of a general peritonitis, the Fowler position and continuous rectal saline irrigation. Rapidity of operation is probably the greatest factor in lessening shock and contributing toward success.

In a few cases where it may be found impossible to close the perforation without

too great narrowing of the lumen of the bowel, enterostomy should be done. In twenty cases of Patterson's series where enterostomy was performed, the mortality was 55 per cent., while in three, where resection was done, it was 100 per cent.

The differential diagnosis from other abdominal complications of typhoid might present some difficulty, but most of them also require operation. Acute appendicitis, acute cholecystitis with or without perforation, suppuration of the mesenteric glands, abscesses of the liver, volvulus, intussusception, perforation of a gastric ulcer, peritonitis without perforation, and acute dilatation of the stomach may occur.

The appendicitis may be purely typhoidal, due to similar changes to those in the ileum, or follow any of the types of appendicitis occurring independently of typhoid. The mortality of twenty-two operations for appendicitis during typhoid was 18.18 per cent. (Patterson). The consensus of opinion, and best advice, appears to be: Do not operate when the appendicitis occurs early in the disease, and only shows mild symptoms, Kelly (10) and Murphy (11), and at the height of the disease do not operate except in the presence of pus or perforation, Deaver (12).

Acute cholecystitis occurring during typhoid is probably more common than is generally believed, as operations are reported much more frequently since attention has been called to the subject. In 1907, Thomas (13) collected 154 cases, with eleven operations. In April, 1908, Ashhurst (14) reported twenty-one operations, and in June, 1908, Quenu (15) reported thirty operations. Since then, the writer, in an incomplete review of the literature, can add six more operative cases, including one case operated on by himself.

The diagnosis is made by the localization of the pain, tenderness, and rigidity, by palpation of the distended gall bladder, and the elevation of the pulse and temperature. Severe cholecystitis, especially where rigidity over the gall bladder is a prominent symptom, calls for operation, as gangrene or perforation is apt to occur. Of Thomas' 154 cases, in the eleven on whom operation was performed, the mortality was 54.6 per cent. In the non-operated cases, 71.9 per cent. In Ashhurst's series of twenty-one cases, the mortality was 61.9 per cent. In Quenu's series, 64.4 per cent., although in twenty of these cases, where a cholecystostomy or cholecystectomy was done, it was only 25 per cent., the larger total mortality being caused by a number of cases where an improper diagnosis, or incomplete operation, due to the condition of the patient, lessened the prospect of a cure. The same is true of Ashhurst's statistics. In the six additional cases found by the writer only one died as a result of the cholecystitis or the operation, but two died subsequently, one of intestinal perforation and the other of pulmonary hemorrhage due to tuberculosis. The treatment is cholecystostomy or cholecystectomy. The former, in a moderately thin patient with distended gall bladder, can be done quite easily with local anæsthesia.

The other abdominal complications previously mentioned require operation, but are rare, and their symptomatology and treatment are the same as if they occurred independently of typhoid, and the scope of this paper does not admit of their individual consideration.

In conclusion, it may be said that, while typhoid belongs within the scope of the internist, much of the mortality of the disease is due to surgical complications. That while the operative mortality, especially of the abdominal complications, is necessarily large, it is much less than if the same cases were treated without operation. That the earlier the diagnosis is made, and the necessary operation performed, the less that mortality will be. And that the best interest of the patient will be attained by early consultation with the surgeon, when there is the first question of a surgical complication, rather than by waiting until it is definitely decided that an operation is necessary.

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SHORT-DURATION TYPHOID FEVER.*

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The term short-duration typhoid fever is used to include the types of the disease which have been designated ambulatory, abortive, mild, typhus lævis, and typhus lævissimus. These types are not well defined, and it seems desirable to have a term which not only will include them all, but at the same time will point out the very important fact that many cases of typhoid fever do not run the classical twenty-one day course. The mild and ambulatory cases come within the meaning of the term only when they last less than three weeks.

Every year during the typhoid season a limited number of patients enter the second medical division of Bellevue Hospital suffering from a mild febrile disease, without obvious cause, which completes its course in periods varying from about one to about two weeks. During the first years of my service at the hospital, in accordance with accepted beliefs, I regarded these cases as examples of febricula or simple continued fever. In 1901, however, when I undertook with Buxton to study the bacteriology of the blood in typhoid fever, I began to question the correctness of this diagnosis. About this time the paratyphoid infections attracted the attention of numerous investigators in Europe and in this country, and the claim was made by several writers that the paratyphoid could be distinguished clinically from the typhoid cases by their milder and shorter course. With the double purpose of testing this claim and of determining the true nature of the disease or diseases in question, we made bacteriological examinations of the blood of all patients who might be suffering from typhoid fever. The recovery of the typhoid bacillus in pure culture from the blood of several of these cases convinced me that the whole question of the occurrence and diagnosis of the irregular forms of typhoid fever might be profitably investigated.

Review of the Literature—Though typhoid fever has been known as a distinct disease for nearly a century, a review of the literature reveals an astonishing state of confusion concerning the very existence of the milder and shorter forms. The history of the diagnosis of typhoid fever falls readily into two periods: (1) The period before the introduction of exact methods of diagnosis; and (2) the period since the application of the Gruber reaction by Widal to the diagnosis of typhoid fever and the general employment of bacteriological methods in the diagnosis of the disease.

First Period—While the diagnosis of a typical case of typhoid fever ordinarily presents no difficulty, supposedly typical cases have occasionally turned out to be acute general tuberculosis. There is no clinical means by which the diagnosis of typhoid fever can be positively established. Therefore the diagnosis of the disease in this period was necessarily a matter of opinion. In a disputed case the diagnosis could not be proved or disproved unless some typical or fatal complication developed and the case came to autopsy. Ordinarily the "weight of authority" prevailed in doubtful cases.

The fact that mild forms of typhoid fever did occur, however, was known very early in the history of the disease. Louis (2) saw a case of ambulatory typhoid which perforated and came to autopsy. These forms were described by Wegelin (3) in 1854, by Griesinger (4) in 1864, by Murchison (5) in 1873, and by Liebermeister (6) in 1874. In 1873 Jurgensen (7) said that the whole theory of infective diseases is untenable if the existence of milder forms cannot be shown; that transitions from the mildest to the severest must be demonstrated.

Yet during the same period there grew up an extensive literature on mild fevers which were not generally, at least, considered to be typhoid and upon which a variety of names were bestowed. Some of these names may be cited: febricula, simple continued fever, mountain fever, "New York fever," embarrass gastrique febrile, fièvre bilieuse simple ou inflammatoire, gastrisches Fieber, and febris gastrica. Fortunately, these names have given place largely to more exact diagnosis. But for many years it was claimed by English army surgeons that there was no typhoid fever in India. As late as 1897, the late Sir Joseph Fayrer (8) stated that "enteric fever occurs in India as it does in Europe, and most probably has always existed there. It may have been confounded with continued or remittent malarial fever, but it is not by any means certain that a febrile condition accompanied by diarrhœa, Peyerian ulceration,

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and an abdominal eruption is necessarily caused by the one specific contagium to which it is attributed in Europe." (At the time this was written the para-typhoid infections had not been studied). In the same article the fever morbidity returns for 1892 of the European and native armies in India, numbering nearly 200,000 men, are given: they were 1,563 cases of typhoid fever, 96,226 cases of intermittent, 2,260 of remittent, and 5,618 *cases of simple continued fever.*

Likewise, for many years it was denied by the French army surgeons that typhoid fever existed in Algeria, but Scherb (9) states that typhoid fever is more common in Algeria than in Paris. Denis (10) says that typhoid fever in the corps in Algeria is almost as great as in the whole army in France.

It is true that the existence of these fevers as distinct diseases was called into question from time to time. Bäumler (11) said in 1867 that the earlier German idea that there existed a "febrile gastric catarrh" as a distinct and not uncommon disease, which in fully developed form was considered "gastric fever," had been gradually abandoned in favor of the belief that it was typhoid fever. Levy (12) in 1886, and Chantemesse (13) and Courtet (14) in 1889, expressed the opinion that embarrass gastrique febrile was a mild form of typhoid fever.

Undoubtedly one reason for the reluctance of the medical profession to accept, during this period, the belief that the milder forms of typhoid fever occurred frequently was the weight of Wunderlich's (15) dictum, issued in 1868, to the effect that a case of fever, without obvious cause, was certainly not typhoid unless the temperature reached 103.2° between the fourth and sixth days. In the absence of exact methods of diagnosis, one might doubt but not disprove the truth of this dictum As late as 1897, Dreschfeld (16) referred to it as still possessing value in diagnosis.

Second Period—The second period opens with the announcement by Widal (17) of his application of the Gruber reaction to the diagnosis of typhoid fever. Strange as it may seem, when one considers the epidemiological importance of the subject, the study of the milder forms of typhoid fever, with the aid of exact methods of diagnosis, has been greatly neglected.

Shortly after the appearance of Widal's paper it was demonstrated in France and Tunis by Lemoine (18), Catrin (19), Geraud and Remlinger (20), and Roux (21) that serum from cases of embarrass gastrique febrile gave the typhoid reaction. Woodruff (22) showed that this was also true for mountain fever in this country. (It may be stated parenthetically that these results would not be accepted to-day because the methods of performing the tests have since been shown to be unreliable. Yet these investigations marked a definite advance in the study of typhoid fever.)

In 1904, during the typhoid epidemic in and around Saarbrück, Koch and his coworkers established the typhoid nature of many mild febrile cases of indefinite clinical character. For example, Drigalski (23) obtained a positive typhoid reaction 306 times and recovered the typhoid bacillus from the stools 75 times in 381 doubtful cases. Frosch (24), by the employment of the same methods, discovered 144 cases of typhoid fever in a region where only 8 had been officially reported.

J. P. Bates has published the results of a study of 68 cases of typhoid fever in Panama (25). Twenty-one (32 per cent.) of the cases were of the short-duration variety. The typhoid bacillus or a paracolon bacillus was recovered from the blood in 9 of these cases; in the 12 remaining cases the diagnosis was based upon the serum reaction. A paracolon bacillus was found in the blood of the case of shortest duration (eight days).

Except for the reports by Debrie (26) and Briggs (27) these are the only papers I have been able to find in which the attempt is made to prove that the milder forms of typhoid fever have often been concealed under the names simple continued fever, mountain fever, etc. A number of papers have been written in which the authors express the belief that the short-duration typhoid fever is of common occurrence and often overlooked, but they either offer no proof or relate only one or two cases.

No paper has yet been published on the bacteriology of the blood in the milder forms of typhoid fever. Buxton and I (28) analyzed the reports of 1,602 cases whose blood had been examined bacteriologically, and the only reference we found to the subject was a brief paragraph by Conradi (29) stating that he had recovered the typhoid bacillus twice from the blood of cases lasting about eight days each.

The Bellevue Hospital Cases—We do not see many of the milder forms of any disease in Bellevue Hospital. Nevertheless, in the last five years, exclusive of 1908, 10 per cent. of 229 cases of typhoid fever on the second medical division have been of the short duration variety. The proportion of mild to severe cases has varied in different years; thus, in 1903 there were only 2 mild cases; in 1904, 11 cases (constituting for that year 25 per cent. of the typhoids); in 1905, 4 cases; in 1906, 5 cases; and in 1907, 2 cases. The febrile period in 9 of the 24 cases lasted about two weeks, in 9 it lasted ten days, in 4 it lasted nine days, and in 2 cases it lasted five and six

days respectively. One of the two cases which occurred in 1903, and which lasted nine days, gave Bacillus coli in pure culture in the blood, but I think it may with propriety be included here (30). The diagnosis in 20 of the 24 cases is not open to doubt, since it rests either upon a positive serum reaction or upon a positive blood culture. In the remaining 4 cases the diagnosis was made upon clinical evidence, it having been impossible for various reasons to study the cases thoroughly, and it therefore is doubtful.

The serum reaction was negative in 6 cases of the series, but in 2 of these the typhoid bacillus was obtained in pure culture from the blood. In 3 of the negative cases blood cultures were not made. In the remaining negative case a blood culture in broth was also negative.

Blood cultures were taken in 19 of the 24 cases, with a positive result 9 times and a negative result 10 times. In one of the negative cases the blood was not taken until after the temperature had reached normal, and according to our prsent experience would not be expected to contain the bacilli. The bacillus was not found in the blood in any case of less than nine days' duration. Conradi's bile medium was used in only two of the negative cases, the other negative cases having been studied before this medium was recommended. As we have had about 97 per cent. of positive results with the bile medium in all varieties of typhoid fever, and have been much less successful with broth, we do not feel that the negative cases in which broth was used are entirely reliable.

Symptomatology—The symptoms of short-duration typhoid fever have been so well described by several authors, notably Curschmann (31), that I shall not discuss them. The temperature curves (Figs. 1, 2 and 3) will show in a general way the course of several of the Bellevue cases.

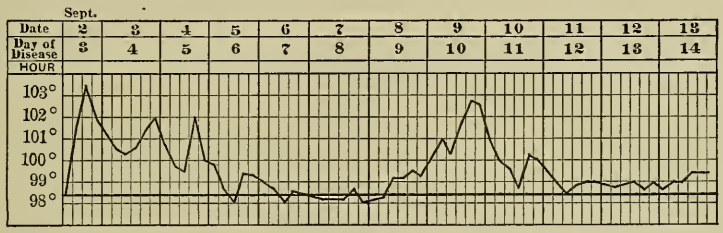

Fig. 1.—Herman R., typhoid fever of seven days' duration, with relapse; positive typhoid serum reaction; blood culture negative.

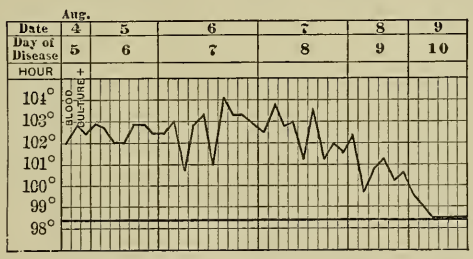

Fig. 2.—Terence B., typhoid fever of ten days' duration; typhoid bacillus obtained from the blood.

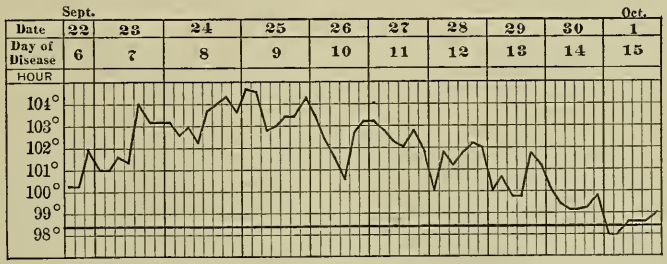

Fig. 3.—Dennis C., typhoid fever of fourteen days' duration; typhoid bacillus obtained from the blood.

Diagnosis—If one may judge of the attitude of the medical profession toward short-duration typhoid fever from current literature and text-books, the conclusion must inevitably be reached that these cases are not often recognized.

Reed, Vaughan, and Shakespeare (32) state their belief "that the number of cases of typhoid fever among the troops of the —— and —— Army Corps was more than twice the number recognized as having that disease." And after a discussion of the mortality statistics of typhoid fever in several of the larger cities of the country, they say (33): "We are forced to conclude that in these cities a large percentage of the cases of this disease are not recognized as typhoid fever. The army surgeon did in his military service just as he was in the habit of doing in his civil practice, *i.e.*, he failed to properly diagnosticate the milder cases of typhoid fever His military record is no worse and no better than was his own record in civil practice or is the record of physicians in some of the larger cities of the United States." The sweeping character of this indictment is startling, but the review of the literature forces the admission that it is not overdrawn. Moreover, this review also shows that the failure to recognize the shorter forms of typhoid fever has not been confined to any one country, but has been world-wide.

Lafforgue (34) says of short-duration typhoid fever: "The true nature of these forms is not often recognized. They constitute one of the most formidable sources of infection."

Turning to the standard text-books, it is found that all of them contain descriptions of the classical case of typhoid fever, with the usual division of the disease into three periods of a week each. Most of them speak of the abortive cases which begin as the longer cases do. Only one of the American text-books gives more than a passing notice to cases which last less than two weeks. Curschmann gives a classical description of these cases, while Dreschfeld says of them only that during epidemics of typhoid fever, when many mild and abortive cases are about, the differential diagnosis from acute gastro-intestinal catarrh may present great difficulty—and leaves the means of overcoming the difficulty to the reader's imagination. The strongest impression conveyed by the text-books is that typhoid fever is a disease of three weeks' duration.

As a final quotation, bearing upon the diagnosis of short-duration typhoid fever, I may cite the title of a paper, by an experienced physician, which appeared in February, 1908. His title is the question, "Is there such a disease as abortive typhoid?" The author believes that there is, but adduces no proof.

When one considers the state of confusion which still exists according to the published opinions of the leaders of the medical profession, concerning the milder forms of typhoid fever, and also the fact that the study of these cases with the aid of the newer laboratory methods has been largely neglected, it is not surprising that practical physicians should hesitate to make the diagnosis of typhoid fever in a case which shows few of the classical symptoms of the disease and which completes its course in two weeks or less. In a recent conversation with a progressive physician from a town of about 12,000 inhabitants, he said he would be disposed to think he had made a mistake in diagnosis if a supposed case of typhoid fever lasted less than two weeks.

But the diagnosis of these cases may easily be made in general practice. It cannot be made clinically except in the presence of some typical complication; one must have recourse to laboratory methods. With dead cultures of the typhoid bacillus, which may be obtained in the market, the serum test may be carried out by any busy practitioner.

Serum Reaction—The fact is well known that a patient's serum may give a positive reaction to the typhoid bacillus when the patient is not suffering from typhoid fever. A positive typhoid reaction means only that the bacillus is growing in the body, and that immune bodies (agglutinins) are forming. Cases of typhoid infection of the biliary passages and typhoid bacillus carriers furnish examples. But if a positive reaction appears transiently during the course of a febrile attack, which is not obviously due to some other cause, the diagnosis of typhoid fever is reasonably certain. It need scarcely be added that to be of value the serum tests must be carefully performed and properly controlled.

The sera of cases of infection by the intermediate members of the typhoid-colon group (the paratyphoid and paracolon bacilli) and by Bacillus coli react only exceptionally to the typhoid bacillus, and should be tested against these organisms. So far as is known at present, however, cases caused by these bacilli constitute but a small proportion of the total typhoids, and except in special instances may be left out of consideration. But it must not be forgotten that epidemics of typhoid fever have been caused by the paratyphoid bacilli. Friedel (35), Lempke, Schottelius (36), Kutscher (37).

Negative serum reactions possess no diagnostic value unless they are obtained daily throughout the febrile period of the disease and well into convalescence. In some of the Bellevue Hospital cases agglutinins were present in the blood for only one or two days, and if the reactions had not been tested on those days the results might have been considered negative throughout.

Bacteriological Examination of the Blood—Bacteriological examinations of the blood cannot be made unless one has access to a well-equipped laboratory, and therefore will not be of much assistance in diagnosis to the general practitioner. However, the method has served the useful purpose of setting at rest all doubt concerning the occurrence of short-duration typhoid fever. According to our experience at Bellevue, the typhoid bacillus is not found in the blood as uniformly in the short-duration cases as in the longer and severer forms of the disease. In several instances as many as three examinations of the blood gave negative results. Positive bacteriological examinations of the stools and urine do not necessarily prove that the patients have or have had typhoid fever. Brown (38) has reported a case of cystitis, caused by the typhoid bacillus, in a patient without a history of typhoid fever. And bacilli of the typhoid-colon group are not infrequently found in the stools of healthy persons—witness the bacillus carriers.

In conclusion, I would say: This study has proved in an incontestible manner that some, at least, of the fevers which formerly would have been considered febricula or simple continued fever are in reality typhoid fever. In the present state of our knowledge it would be rash to assert that all mild fevers in this latitude, for which no other cause can be found, are typhoid in nature, but I can state that we have had no series of cases of mild fevers in Bellevue Hospital in the last five years which could not be proved to be either typhoid fever or some easily recognized disease, as bronchitis, gastro-intestinal disturbance, etc.

This investigation has also brought out the fact that a great deal of confusion exists in the literature concerning the milder forms of typhoid fever, and emphasizes the urgent need, from the epidemiological standpoint, of a more thorough study of these forms. No statistics have been accumulated, since exact methods of diagnosis have come into general use, to show the relative proportion of the mild to the severe cases of typhoid fever. Doubtful cases should be treated as typhoid fever until the cause of the disease can be found.

I would suggest that unless the writers of text-books on medicine, from which students are taught and to which practitioners turn when in doubt, devote more attention to the consideration of the milder forms of typhoid fever, they cannot hope to escape responsibility for a large share of blame for the occurrence of epidemics arising from this source.

Finally, I wish to express my indebtedness and my thanks to Dr. Buxton for making the blood cultures and to Dr. Hastings for performing the serum tests.

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BACILLUS COLI COMMUNIS: THE CAUSE OF AN INFECTION CLINICALLY IDENTICAL WITH TYPHOID FEVER.*

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Cases of infection clinically identical with typhoid fever have been caused by Bacillus fæcalis alcaligenes, the paratyphoid and paracolon bacilli (Bacillus paratyphosus, types A and B), Bacillus enteritiditis, and Bacillus psittacosis. The close biological relationship of these members of the typhoid-colon group (the Typhaceæ, as Loeffler has designated them recently) and the fact that the paracolons are more nearly related to Bacillus coli than to Bacillus typhosus naturally lead to the suspicion that some strains of Bacillus coli also might be capable of causing the typhoid symptom complex. Though there is increasing evidence of variability, and even mutation, of type among the Typhaceæ, a discussion of this phase of the typhoid problem does not come properly within the scope of our paper.

Our attention was first directed to the question of systemic infection by the colon bacillus pursuing a typhoid-like course in 1903, when Buxton and one of us recovered colon bacilli from the blood of two cases in Bellevue Hospital which were considered clinically as examples of mild typhoid fever. These cases were reported briefly on a former occasion:

Case I.—A. F., butcher's helper, entered Bellevue Hospital in the service of Dr. Thompson, August 15, 1903, the eighth day of his illness. He had been swimming daily in the East River. For a week he had suffered from general weakness, frontal headache, pain in the stomach and legs, bad taste in the mouth, and loss of appetite, but in spite of these symptoms had continued at work washing beef tongues in a damp cellar. There had been no vomiting or diarrhœa.

On admission the patient's tongue was coated and tremulous. The spleen was not palpable. About two dozen rose spots were found upon the chest and abdomen. The general appearance of the patient suggested mild typhoid fever. Fresh rose spots appeared on August 17, but by the 20th all the spots had disappeared. The temperature on admission was 100.4 degrees Fahrenheit; pulse, 96. Thereafter the temperature gradualy fell and reached normal on the twelfth day of the disease. The patient's serum was tested against the typhoid bacillus on the tenth and twelfth days, microscopically in dilution of 1 to 100, both times with negative results after two hours. Unfortunately the reaction of the serum against the colon bacillus was not tested. On the tenth day of the disease 10 c. c. of blood, taken from a vein at the elbow contained a colon bacillus in pure culture. August 30, after twelve days of normal temperature, a relapse occurred. During the relapse the temperature rose to a maximum of 101 degrees Fahrenheit. The duration of the relapse is unknown, since on September 14, thirty-eight days after admission, the patient insisted on leaving the hospital with a pulse of 120 and a temperature of 99.5 degrees Fahrenheit.

Case II.—B. McM. Occupation, housework. Entered Bellevue Hospital August 14, 1903, in the service of Dr. Thompson, complaining of severe general headache, dry cough, pain in the back and sides, loss of appetite, and constipation. She had a temperature of 101.4 degrees Fahrenheit and a pulse of 100. A clinical diagnosis of mild typhoid fever was made. On the sixth day of illness her serum, in dilution of 1 to 100, was negative microscopically to the typhoid bacillus after two hours. Two days later her blood was found to contain a colon bacillus in pure culture. But the following day her serum gave a positive Widal reaction at 1 to 100. The reaction against Bacillus coli was not tested.

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According to present standards, the data concerning Case II. are too meager to permit our drawing any conclusion regarding it. We are unable to determine whether the case should be considered as one of primary systemic infection with a colon bacillus, exhibiting a group reaction against the typhoid bacillus, or whether to look upon the presence of the Bacillus coli in the blood as a secondary invasion. The former seems the more likely when one considers the small number of patients whose blood has contained Bacillus coli communis during life, and the very infrequent association of Bacillus typhosus and Bacillus coli in the blood of typhoid cases.

Case I., on the other hand, meets the requirements more fully; that is, (1) it was clinically mild typhoid fever, (2) Bacillus coli communis was obtained in pure culture from the blood, and (3) the serum reaction was negative to the typhoid bacillus as late as the last day of the fever in the primary attack. It would have added to the completeness of the data if the patient's serum had been tested against several stains of Bacillus coli, but this was not done. With these cases in our possession, a search of the literature for similar ones was undertaken.

In 1902 Fox recovered a colon bacillus from the blood of a case which resembled typhoid fever clinically. The serum of the patient gave a positive Widal reaction on the thirty-second day of the disease, though it had previously been negative. Therefore, as in Case II. above, the true nature of the infection was doubtful.

In the same year Burch write, under the title of "Colon Bacillus Infection," that for ten years he had seen in his practice cases of fever, lasting from seven to ten days, which were ushered in by malaise, a gradual rise of temperature to a maximum of 103 degrees to 104 degrees Fahrenheit by the third or fourth day, diarrhœa, or, less frequently, constipation. The tongue was dry and often coated. Sometimes there was mild delirium; there was always more or less headache. Tympanites occurred in some cases. The whole clinical picture was that of typhoid fever. The leukocytes were diminished in all cases. The urine was always acid and many times swarmed with motile organisms resembling Bacillus typhosus. The diazo reaction was, as a rule, well marked. The Widal reaction, made daily (dilution approximately 1 to 5), was absent in every case throughout its course, but the serum reacted promptly to the organism obtained under aseptic conditions from the bladders of the patients. This organism responded to all the cultural tests for Bacillus coli communis. This remarkable series of cases was observed in Baldwinsville, New York. While the nature of the infection cannot be accepted as proved, the cases appear to have been what the author considered them, examples of colon bacillus infection pursuing the course of typhoid fever.

In 1903 three papers appeared upon this subject. Evans and Sailer reported the case of a negro who, on February 12, suddenly became weak and dizzy. Next day he had diarrhœa, loss of appetite and gastric disturbances. The spleen was palpable. Rose spots were present. The disease ran the course of typical typhoid fever. The temperature became normal on March 6. A relapse occurred which lasted to the 16th. The leukocytes on February 15 numbered 5,900; February 17, 10,480; March 9, 7,000. The diazo reaction was positive in the first part of the illness. The serum tests upon which the diagnosis rests must be given in detail: Against Bacillus typhosus the reaction was positive at 1 to 10 on five occasions, while it was negative at higher dilutions. Against Bacillus paratyphosus (four strains), the reaction was incomplete at 1 to 10 on the twentieth day of the disease, but it was positive at 1 to 10 on the forty-third day of the disease. Against Bacillus coli communis (Pasteur Institute culture), the reaction was complete in forty-five minutes at 1 to 100 on the twentieth day. On the forty-third day, the reaction was complete at 1 to 150 in one hour, partial at 1 to 200 and 250 in one and a half hours (no increase later), and negative at 1 to 300 and 1 to 400 after twenty-four hours. The case, therefore, appears to have been caused by a colon bacillus.

A. Jacoby, of New Orleans, reported a case which he considered especially interesting because it resembled typhoid fever so closely: A laborer, fifty years of age, was working on a railroad in Texas when he was taken ill. He had drunk any water he could get. There had been no diarrhœa. The temperature on admission to hospital was 101 degrees Fahrenheit; pulse rapid. The abdomen was distended. The spleen was much enlarged. Rose spots were present. No malarial organisms found. The Widal reaction was negative four times (dilutions and days not stated). Rose spots and the urine were examined for Bacillus typhosus with negative results. Bacillus coli communis was present in the urine in large numbers. After admission the temperature did not rise above 102 degrees Fahrenheit, and in a week began to decline. On the sixteenth day, however, double lobar pneumonia developed, the temperature rose suddenly to 104 degrees Fahrenheit, and death followed. At autopsy,

the small intestine was congested throughout its extent, but Peyer's patches were not involved.

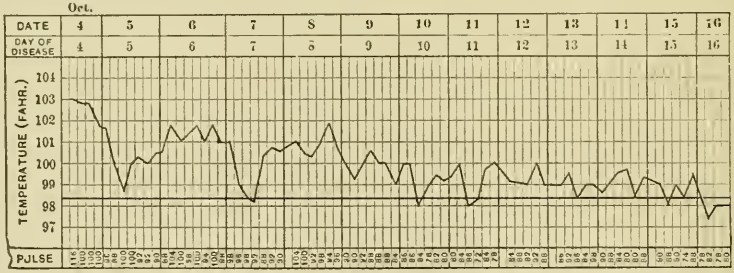
Bauermeister reported the case of a man, thirty-five years of age, from whose blood he obtained Bacillus coli communis in pure culture on several occasions; he regarded the case clinically as typhoid-like in its course. Similar attacks recurred over a period of one and one-half years, when one of the patient's testicles had to be amputated because of an abscess which contained Bacillus typhosus. Bauermeister suggests that the original colon bacillus had changed its biological characters probably as the result of long residence in the body. This case seems to us to belong with the colon bacillus septicemias rather than in the typhoid group which we are discussing.

In 1904 Widal and Lemière reported two cases, which they state resembled typhoid fever, and from whose blood they recovered colon bacilli. As their second case showed multiple abscesses of the kidney at autopsy, it cannot be included in the present series. Their third case occurred in a man, thirty-five years of age, who was taken ill suddenly five days before admission to the hospital with violent abdominal pain, repeated chills, and vomiting. He had almost constant headache and complete insomnia after the onset. There was no epistaxis or diarrhœa. The temperature on admission was 103.5 degrees Fahrenheit; pulse 90. There was marked abdominal distention. No rose spots. Spleen voluminous. Violent intestinal peristalsis. Heart, lungs and liver normal. The abdominal pain and tenderness disappeared. Diazo reaction negative. Serum, negative to the typhoid bacillus. The patient's illness lasted from December 12 to December 21. He was discharged from the hospital December 24. On December 18 a colon bacillus was obtained in pure culture from 3 c.c. of blood. December 24, the patient's serum agglutinated his own bacillus at 1 to 30.

These are the only cases we have been able to find, reported as cases of systemic infection by the colon bacillus, pursuing the course of typhoid fever, which will bear analysis.

In the fall of 1905 we were fortunate enough to have the privilege of studying the following case:

Case III.—G. K., twenty-nine years of age, entered Bellevue Hospital October 4, in the service of the late Dr. Loomis. He had been in Central America for a year and a half, where he contracted malaria and yellow fevers. Early in July he spent eight days in Jamaica, en route to New York, where he has remained since August 24. During this time he has been well. The present illness dates from September 30, when he felt feverish. He waked next morning with a headache, mainly frontal and occipital; pain in the muscles of the neck on moving the head, and pain in the right knee and arm. Walking was difficult. In spite of these symptoms, the patient went to his office, where he remained until afternoon. On the way home he felt very weak.



Temperature Chart of Case III (G. K.).

When he got into bed, he had a chill, lasting twenty minutes, followed by sweating. The headache continued, and pains developed in the back. Three days after the first chill he had another (October 3) lasting ten minutes. His head and hands became very hot, but he did not sweat. October 4 he felt so weak that he decided to remain in bed. His bowels had not moved since October 1. For several days he had had a dry, hacking cough. In the afternoon, when he entered the hospital, he was chilly and suffered from nausea and vomiting.

Physical Examination—The patient is a well-nourished, well-developed man. Face flushed, skin dry, but in good condition. Tongue large, flabby, coated, and tremulous. Heart and lungs normal. Arteries not thickened. Slight abdominal distention. Slight tenderness in left upper quadrant of abdomen. Liver normal. Spleen

not palpable. A few rose spots on the abdomen. The clinical picture is that of mild typhoid fever.

Subsequent History—October 5, headache and abdominal pain all night. Slept about two hours. Fresh crop of rose spots. The spots continued to appear at intervals until the 16th. Slight bleeding when the patient blew his nose. From the 6th to the 9th the patient complained chiefly of vague abdominal pain and headache.

October 9—Conjunctivæ and skin slightly icteric.

October 10—Pain in right hypochondrium (heretofore the pain was not localized). Marked jaundice. Tenderness over gall-bladder. Spleen percuses large, but cannot be felt.

October 11—Jaundice deeper. Tenderness over gall-bladder more marked. Nausea. Severe frontal headache.

October 12—Gall-bladder exquisitely tender. Spasm of overlying muscles. Patient brighter.

October 14—Gall-bladder palpable. Extends one and three-fourths inches below free border of ribs.

October 16—Gall-bladder less tender. Jaundice beginning to clear up.

Thereafter the jaundice gradually disappeared, the gall bladder receded, and tenderness was developed only on deep pressure. This tenderness persisted, however, until October 27, and for months afterward the patient had a sense of discomfort on bending over. The patient was discharged from the hospital as cured on November 17.

Cytological Examinations of the Blood—October 4. Leukocytes, 5,000; polynuclears, 62 per cent.; lymphocytes, 24 per cent.; large mononuclears, 8 per cent.; transitionals, 4 per cent. No malarial organisms.

October 5—Leukocytes, 6,000; polynuclears, 77 per cent.; lymphocytes, 14 per cent.; large mononuclears, 8 per cent.; eosinophiles, 1 per cent.

October 9—Leukocytes, 6,400; polynuclears, 45 per cent.; lymphocytes, 29 per cent.; large mononuclears, 6 per cent.; transitionals, 18 per cent.; eosinophiles, 5 per cent.; mast cells, 0.3 per cent.

October 10—Leukocytes, 8,000; polynuclears, 66 per cent.; lymphocytes, 20 per cent.; large mononuclears, 10 per cent.; transitionals, 2 per cent.; eosinophiles, 4 per cent.

Two blood cultures in broth were made October 5 and 9, but both proved negative (Buxton).

Three rose spots were examined bacteriologically with negative results (Buxton).

The urine was examined bacteriologically twice and found negative (Buxton, Warren).

The feces were examined three times for Bacillus typhosus or any of the intermediates, and also found negative (Norris, Buxton).

AGGLUTINATION REACTIONS*. AGAINST BACILLUS TYPHOSUS.

October 9, 10, 13, 14, 16, 18, 19:
Microscopically, in dilution of 1 to 50, negative after two hours.
Macroscopically, in dilution of 1 to 100, negative after twenty-four hours.

October 21:
Microscopically, in dilution of 1 to 50, negative after two hours.
Macroscopically, in dilution of 1 to 100, negative after twenty hours.
Macroscopically, in dilution of 1 to 200, negative after twenty hours.

October 23:
Microscopically, in dilution of 1 to 50, negative after two hours.
Macroscopically, in dilution of 1 to 100, negative after twenty hours.
Macroscopically, in dilution of 1 to 200, negative after twenty hours.
Macroscopically, in dilution of 1 to 400, negative after twenty hours.

October 24:
Microscopically, in dilution of 1 to 50, negative after two hours.
Macroscopically, in dilution of 1 to 200, negative after twenty hours.
Macroscopically, in dilution of 1 to 20, negative after twenty hours.

AGAINST BACILLUS PARATYPHOSUS (TYPES A AND B).

October 14:
Macroscopically, in dilution of 1 to 10, positive after twenty hours.

October 18 and 19:
Macroscopically, in dilution of 1 to 100, negative after twenty hours.

* The dilutions stated are the dilutions of the serum before admixture with the suspension of bacilli—the final dilutions, therefore, would be twice as high.

October 21:
Macroscopically, in dilution of 1 to 100, negative after twenty hours.
Macroscopically, in dilution of 1 to 200, negative after twenty hours.
October 23:
Macroscopically, in dilution of 1 to 100, negative after twenty hours.
October 24:
Macroscopically, in dilution of 1 to 200, negative after twenty hours.
Macroscopically, in dilution of 1 to 20, negative after twenty hours.

AGAINST BACILLUS COLI (STRAIN A).

October 14:
Macroscopically, in dilution of 1 to 20, positive after twenty hours.
October 18 and 19:
Macroscopically, in dilution of 1 to 100, positive after twenty hours.
October 21:
Macroscopically, in dilution of 1 to 200, positive after twenty hours.
October 23:
Macroscopically, in dilution of 1 to 400, positive after twenty hours.
October 24, 26 and 28:
Macroscopically, in dilution of 1 to 200, positive after twenty hours.
October 30 (strains A and B):
Macroscopically, in dilution of 1 to 200, positive to A after twenty hours
negative to B after twenty hours.
November 1:
Macroscopically, in dilution of 1 to 100, positive to A after twenty hours.
Negative to B after twenty hours.

November 15, the serum in dilution of 1 to 100 was tested against seventeen strains of Bacillus coli, including strains A and B previously used.

The reactions were positive with strains 2, 6, 13 and A.

December 29, the serum no longer agglutinated any strain of Bacillus coli in dilutions of 1 to 100 and 1 to 20.

All of the reactions above noted were end-reactions—tests with more dilute serum proving negative.

While we are aware that we have not proved *beyond doubt* (through our failure to recover the colon bacillus from the blood) whether G. K.'s. infection, was local (that is, a colon bacillus cholecystitis) or general, we are convinced that we have proved that the disease was not caused by Bacillus typhosus or any of the intermediates. The case was considered clinically to be mild typhoid fever by all who saw him, including the late Dr. Loomis and Dr. Thompson. Nevertheless, to forestall criticism, it will be well to discuss the clinical differential diagnosis.

The various clinical possibilities seem to have been: (1) Clinical typhoid fever, complicated by cholecystitis. (2) Primary cholecystitis. (3) Tuberculosis. (4) Sepsis. (5) Pyelitis.

The condition of the urine throughout the disease excludes pyelitis.

The course of the disease and the subsequent history exclude sepsis and tuberculosis (the patient was not lost sight of until the fall of 1907).

There remain only the two varieties of cholecystitis, catarrhal and suppurative. Suppurative cholecystitis may be excluded for the same reasons as sepsis. As against a primary catarrhal cholecystitis caused by the colon bacillus, we base the clinical diagnosis of a typhoid-like fever upon the following facts: mode of onset with the gradually developing malaise, initial chills, slight bronchitis, slight epistaxis, persistent headache, appearance of rose spots on the fifth day of the disease, the course of the disease, the emaciation, and the phenomena of convalescence. Leukopenia, with a low polynuclear count, was present until the day after the cholecystitis became evident clinically. The leukocytes then rose to 8000 and the polynuclears from 45 per cent. to 66 per cent. Though there had been previously vague abdominal pains, these are not uncommon in typhoid fever. Definite tenderness over the gall-bladder did not develop until the day following the subicteric tinging of the conjunctivæ and skin. We are very positive in this statement, because for years it has been our habit to examine daily the gall-bladder region of all patients in the wards suffering from typhoid fever. From all of these considerations we feel justified in thinking that the case of G. K. was clinically typhoid fever, complicated by cholecystitis.

In order to make this study as complete as possible, we have sought during the last three years to obtain the serum of cases suffering from a colon bacillus cholecystitis for the study of its agglutination reactions, but unsuccessfully. We have also written to prominent surgeons to obtain such data, but none of them could furnish

the desired information. The literature is silent upon this point. The development of immune bodies for various strains of Bacillus coli in cases of cholecystitis caused by this bacillus offers an interesting and important field for study.

Though it is well established that Bacillus coli may enter the blood during life, only a limited number of cases have been reported in which this fact has been demonstrated by blood culture. Most recent writers on localized colon bacillus infections, for example, of the gall-bladder and of the kidney and its pelvis, recognize the systemic blood stream as one of the channels of infection (Lenhartz, Lockwood, Brewer). While in most of these cases it is probable that the bacillus is only transiently in the blood, Lenhartz and Schmeidemandel have reported cases in which the bacillus has been obtained by blood culture.

A limited number of cases of colon bacillus septicemia have been reported (Bertelsmann and Mann, Lenhartz, Sittman and Barlow, Albarran, Libman, De Gennes and Hartmann, Hitschmann and Michel, Stern, Stadelmann and Wolff-Eisner, Fehling, Blackader and Gillies).

With the possibility of the entrance of the colon bacillus into the blood during life proved, it seems to us, that it need excite no surprise that some strains of this bacillus in view of their close resemblance to some of the paracolons, may cause under certain conditions a disease clinically identical with typhoid fever. Buxton and one of us have suggested that even Bacillus typhosus is incapable of causing typhoid fever unless it develops in the general lymphatic system, including the spleen and bone-marrow, and thence invades the blood, where it is destroyed in large numbers. Localized infections with Bacillus typhosus do not cause typhoid fever. Lentz thinks that the same conditions of infection obtain in the typhoid-like types of paratyphoid infection. While there is no direct evidence to offer, from analogy it is probable that when a colon bacillus causes the symptoms of typhoid fever, the distribution of the bacillus in the body is the same as in the case of typhoid and paratyphoid infections.

Discussion of the Agglutination Reactions for Bacillus Coli—The blood examinations in Cases I. and II. of the Bellevue Hospital series have been noted in the clinical report. The presence of Bacillus coli in blood taken from a vein leaves no doubt as to the bacteremia, and we feel inclined to accept this as evidence that this bacillus was the cause of the infection. No tests for immune bodies (agglutinins) were carried out.

In Case III., G. K., blood taken from a vein on two occasions proved sterile, and the supposition that Bacillus coli communis was the cause of the infection is based upon the facts that immune bodies (agglutinins) for a certain strain of Bacillus coli were found in the blood during the febrile period and were not found after recovery, and that the same strain of Bacillus coli was not agglutinated by many other sera in high dilution, thus fulfilling our own ideas of the diagnostic value of agglutination reactions and coinciding with the results of Klienberger.

	Oct. 10, 1905, 1–50 to 1–100.	Oct. 12, 1–100.	Oct. 14, 1–100.	Oct. 21, 1–200.	Oct. 23, 1–400.	Oct. 24, 1–400.	Oct. 26, 1–100.	Oct. 28, 1–200.	Oct. 30, 1–200.	Nov. 1, 1–100.	Nov. 15, 1–100.	Dec. 29, 1–100 to 1–20.
Bacillus typhosus	—	—	—	—	—	—	..	..	..	..	—	—
Bacillus paratyphosus A and B	..	..	—	—	..	..	..	..	..	..	—	—
Bac. coli A	..	..	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+	—
Bac. coli B	..	..	—	—	..	..	..	..	—	—	—	—
Bac. coli No. 2, No. 6, No. 13.	..	..	..	..	..	..	..	..	..	..	+	+
Bacillus coli, 12 strains	..	..	..	..	..	..	..	..	..	..	—	—

Dilutions refer to the diluted serum; final mixtures were twice the serum diluted.

Agglutination tests in Case III. gave the following results: October 10 and 12, tests against Bacillus typhosus were negative in dilutions 1 to 50 and 1 to 100. October 14, the serum diluted 1 to 100 was tested against Bacillus typhosus, Bacillus paratyphosus (A and B), and one strain (A) of Bacillus coli, and the reaction for strain A Bacillus coli was positive; for the other organisms, negative.

Control tests were carried out with strains of Bacillus typhosus, Bacillus paratyphosus, and certain negatively reacting Bacillus coli strains, and the reactions noted were end-reactions—tests with more highly diluted serum proving negative.

The macroscopic method, with fresh emulsions prepared after Borden's method, was used, and also fresh suspensions in 0.8 per cent. sodium chloride solution. October 21, the serum diluted 1 to 200 gave the same positive reaction against strain A Bacillus coli. October 23, the serum diluted 1 to 400 was positive for A. October 24, 26 and 28, serum diluted 1 to 200 was positive.

October 30 the serum was tested against strains A and B Bacillus coli and proved positive to strain A and negative to strain B, in dilution 1 to 200. November 1, the same reactions as on October 30 were obtained in dilutions of 1 to 100.

November 15, the serum diluted 1 to 100 was tested against 17 strains of Bacillus coli, including strains of A and B used previously.

The reactions were positive with strains 2, 6, 13 and A. December 29, the serum no longer agglutinated any of the Bacillus coli strains in dilutions of 1 to 100 and 1 to 20.

Bacillus coli strain A which constantly agglutinated with the serum diluted 1 to 100 from October 14 to November 15, and 1 to 400 October 23, had been obtained from one of the Bellevue cases above cited (1903). Strains 2, 6 and 13, which the serum, diluted 1 to 100, agglutinated November 15, had been obtained from the blood and the stool of a case of colon bacillus septicemia. Strain 6 was obtained from the ureter of a case of pyelitis. Therefore the serum of G. K. agglutinated 4 strains of Bacillus coli obtained from three different individuals.

For the various strains of Bacillus coli and Bacillus paratyphosus we were indebted to the laboratories of Drs. Buxton and Elser.

In connection with the study of Case III. we have made numerous tests of the serum reactions of non-icteric and icteric cases.

Non-icteric Cases—During the typhoid seasons of 1905, 1906 and 1907, 100 serum tests on 54 cases were carried out against Bacillus coli (strains A, B and 2) and Bacillus paratyphosus (strains A and B).

The serum of a normal individual, used as a control, and the sera from 52 febrile cases, many of them Bacillus typhosus infections, were found negative to Bacillus coli (strain A) in dilutions above 1 to 20, with one exception. The serum from one febrile case, diluted 1 to 20, agglutinated Bacillus coli (strain A), and the serum from two cases, diluted 1 to 20, agglutinaed Bacillus paratyphosus strains, but did not agglutinate Bacillus typhosus or Bacillus coli strains.

The sera from 31 cases did not agglutinate any one of several strains of the typhoid-colon group.

The sera from 16 cases agglutinated Bacillus typhosus, but not Bacillus paratyphosus and Bacillus coli strains.

Unfortunately, in 40 cases single tests only were made: In 6 cases two tests; in 3 cases three tests; in 1 case four tests; in one case six tests; in 2 cases nine tests; in 1 case ten tests; in the cases with six, nine, and ten tests the blood was taken at intervals extending over an entire month.

Cases with Jaundice as a Symptom—The sera of 13 cases with well-marked jaundice as a symptom were tested against strains of Bacillus typhosus and Bacillus coli—single observations n 12 cases and three observations in 1 case. In one instance, a single observation, Bacillus typhosus was promptly agglutinated both microscopically and macroscopically; in a second instance, Bacillus coli (strain B from a pleural exudate) was agglutinated macroscopically in dilution of 1 to 100, but not above; in a third instance, a case of catarrhal jaundice, Bacillus coli (strain 2) was agglutinated with serum diluted as high as 1 to 100.

Thus, none of these cases, with or without jaundice, agglutinated any one of the typhoid-colon group which were tested in dilutions above 1 to 100. In view of the fact that the sera from three jaundice cases were not tested over a period of weeks, we do not intend to discuss these single positive reactions as evidence that a particular strain of Bacillus coli was the infecting agent, although Kelly's paper suggests that such reactions may be of value in this direction.

For Bacillus typhosus it is well known experimentally that the sera of immunized animals must be diluted to the thousands before selective reactions are obtained, while in clinical medicine dilutions of the patients' sera 1 to 50 give diagnostic reactions within certain time limits.

In discussing the agglutination tests for the purpose of diagnosticating a colon bacillus infection, the following types of cases must be considered from theoretical and practical standpoints:

A. Cases of undoubted colon-group infection, in which blood cultures were positive during life and not during the pre-lethal stage or post-mortem. These cases may be divided into two groups:

1. (*a*) Cases which were typhoid-like in course, whose blood contained agglutinins for strains of the colon bacillus.

(*b*) Cases which were typhoid-like, whose blood did not contain agglutinins for strains of Bacillus coli.

2. (*a*) Cases which were not typhoid-like in course, whose blood contained agglutinins for strains of Bacillus coli.

(*b*) Cases which were not typhoid-like in course, whose blood did not contain agglutinins for strains of Bacillus coli. Endocarditis and pyelitis are examples of the last two groups.

B. Cases of supposed colon-group infection, with negative blood cultures. These cases likewise may be divided into two groups:

1. Cases which were typhoid-like in course, whose blood contained agglutinins for strains of Bacillus coli.

2. Cases which were not typhoid-like in course, whose blood contined agglutinins for strains of Bacillus coli. Cholecystitis and pyelitis are examples of this last group.

In the light of our knowledge of group-agglutinins, one must consider the relation of other typhoid-colon group infections to infections by the colon bacillus; for example:

1. Cases of undoubted Bacillus typhosus infection, clinically typhoid-like in nature, in which blood cultures and agglutination tests for Bacillus typhosus were positive and agglutinins for colon stains were found.

2. Cases in which agglutinins were positive for Bacillus typhosus alone, with blood cultures positive for Bacillus coli; or in which blood cultures were negative, and yet agglutinins were found for both typhoid and coli strains.

3. Cases in which blood cultures were positive for Bacillus paratyphosus and agglutinins were found for paratyphoid and colon strains.

4. Cases in which blood cultures were positive for Bacillus coli and whose serum agglutinated typhoid or paratyphoid strains.

Finally, the agglutination of colon strains by normal sera must be considered. The results of Klieneberger show a high agglutinin content for normal serum, diluted 1 to 2,000 to 3,000, for certain colon strains, and would lead one to consider the possibility that some individuals are producers of antibodies for Bacillus coli. Our results are at variance with Klieneberger's in that normal serum and sera from febrile cases have not caused agglutination of colon strains excepting in dilution of 1 to 20 in a febrile case without jaundice, and in dilution of 1 to 100 in two cases with jaundice. This contradiction is readily explained by the fact that in testing 17 different strains of Bacillus coli we found 4 strains only which were agglutinated by 5 out of 67 sera.

The fact that Klieneberger worked with a strain which was agglutinated by many normal sera would not invalidate our results unless it were proved that his colon strain is identical with one or more of those used by us.

Terminal colon bacillus infections and the reactions of typhoid bacillus carriers do not concern us.

Articles in the literature dealing with agglutination tests in Bacillus coli infections are not numerous, yet one or two of them, together with the results obtained in Case III. cover the theoretical and practical consideration in respect to diagnostic reactions.

Klieneberger refers to Pfaundler's statement that the colon bacillus is agglutinated when one mixes together the serum and a strain of Bacillus coli obtained from the same patient, and not when the serum and bacteria are obtained from different individuals under normal conditions. From the work of Wassermann and others it is known that immune coli sera differ not only in respect to the strain used for immunizing, but also according to the type of animal used for immunization, and to explain these differences extensive variation in receptors of different coli strains are supposed to exist. Noting these statements, Klieneberger worked with sera from normal adults, and then from the newborn, with immune coli sera from immunized animals and from a man infected with Bacillus coli. The standard strain of Bacillus coli used was from the urine of a patient with genito-urinary colon bacillus infection. Thirteen other strains of Bacillus coli were selected from 21 strains, for carrying out absorption experiments on sera agglutinating the standard strain. From six newborn infants, the sera being tested against 6 coli strains, 2 sera agglutinated 2 different strains, one each as high as 1 to 160; and the agglutination from 1 strain only was proved by absorption tests. From normal adults with no history of icterus

or typhoid fever, 2 sera, diluted 1 to 1,280, agglutinated 2 strains of Bacillus coli; 4 cases, 1 to 320, agglutinated 3 strains; 1 case, 1 to 640, agglutinated 1 strain. It is noticeable that 2 strains were agglutinated by 5 sera diluted 1 to 320 or over, and that each serum, 1 to 320, agglutinated at least 1 strain. Three strains were not agglutinated by any serum, and 5 strains were not agglutinated by any serum diluted above 1 to 80. No serum agglutinated Bacillus typhosus or Bacillus paratyphosus (A and B) above 1 to 20. One normal serum (M) agglutinated weakly 2 strains, with serum dilutions of 1 to 2,560; 1 strain, with serum dilutions 1 to 640; 1 strain, 1 to 320; 1 strain, 1 to 160; and 3 strains not above 1 to 40. With normal serum M, by precipitation with 8 strains, partial agglutinins were found for 5 colon strains, and with normal serum R, partial agglutinins for 4 colon strains were found; and, further, it was found that one could group the agglutinable strains under two subdivisions, one of which was agglutinated constantly by highly diluted sera and the other irregularly and by low dilution. A second group of coli strains was not agglutinated by any serum. From these observations Klieneberger concludes that a tested strain of Bacillus coli has set up a specific immunity only when we can show that it is agglutinated with abnormally high dilutions, or that normal serum does not agglutinate the strain. He also speaks of an increment in agglutinating power as indicative of immunization from active infection, and cites 2 cases as showing this fact; and he refers to observations on Bacillus coli infections of the urinary tract, during which he had noted the same incremental auto-immunization.

In opposition to Pfaundler, the first fact noted was that in many Bacillus coli infections an agglutinating effect for the causative strain was absolutely wanting. He obtained a "group" agglutination for the typhoid bacillus four times, and for the paratyphoid bacillus once, with the Bacillus coli serum. Klieneberger concludes that in cases of Bacillus coli infection in man, when the causative agent has not been isolated, it is scarcely possible to prove a Bacillus coli infection with serum tests unless immunity to Bacillus coli can be determined, when an increasing agglutination and abnormally high agglutination is found, and normal controls are negative. Further, Klieneberger immunized rabbits against 5 active strains of Bacillus coli with 1 c.c. of a formalized broth culture injected intravenously and obtained a high agglutinating power against the immunizing strain and a much less (1/20 of the high) agglutinating power against 3 non-immunizing strains, and negative results against 8 other Bacillus coli strains, 1 typhoid strain, and paratyphoid strains A and B. A similar chief agglutinin was obtained with the 5 strains used for active immunization.

Case III. (G. K.) illustrates well the increment of agglutination which is essential, according to Klieneberger, for the proof of Bacillus coli immunization.

Mayer found one strain (R) which was usually agglutinated by normal serum diluted 1 to 100 (macroscopic test) and 1 to 250 (microscopic test), and other strains (M, N, L) with which agglutination was not obtained with sera little diluted. Strain M not only did not agglutinate well with normal serum, but was not readily agglutinated by serum (1 to 50) from an animal immunized to strain R, and did not produce agglutinins of any power when used for immunization.

This variation in the agglutinability and in the antigen for agglutinin in certain strains was the most interesting result of Mayer's investigation. Dead bacteria (Bacillus coli, twenty-hour cultures) gave stronger agglutinins and with more certainty than living bacteria when used for immunizing animals, an observation also made by Radzievsky (1900).

Bauermeister's case of general Bacillus coli infection, and later abscess of the testicle, was not carefully studied for agglutinins. An organism isolated from the abscess gave a "Widal" (?) 1 to 50, while the bacilli (Bacillus coli) from the blood and from the urine were not agglutinated; whether with the patient's serum or not does not seem clear. The bacillus isolated from the abscess—one and one-half years after the observations on the blood and urine—did not present the same cultural characteristics as those of the bacilli isolated from the urine and blood.

Jochmann, in 1906, recorded some interesting observations on infections of the urinary tract and general infection with the colon bacillus—two cases with an intermittent fever. In one case, following operation for carcinoma of bladder and subsequent catherization, pneumonic signs developed, and later chills occurred, after which blood cultures with 20 c.c. of blood gave a growth of 10 colonies of Bacillus coli. In a second case, during a cystitis due to Bacillus coli, 8 colonies of Bacillus coli were grown from 20 c.c. of blood. Jochmann considered both these cases a blood invasion by Bacillus coli. In the first case Jochmann tested the agglutinating power of the serum against Bacillus typhosus, Bacillus paratyphosus, and several Bacillus coli strains. No reactions were obtained with Bacillus typhosus and Bacillus

paratyphosus, and one strain of Bacillus coli was agglutinated by serum diluted 1 to 80, and the Bacillus coli isolated from the patient was agglutinated by serum diluted 1 to 160. The patient's strain of Bacillus coli was agglutinated also by sera diluted 1 to 80 from four cases of acute cholelithiasis and by serum, diluted 1 to 320, from a protracted case of cholelithiasis; and a case of icterus with hepatic conditions and cholangitis gave a serum which, diluted 1 to 160, agglutinated the same strain of Bacillus coli. These cases he considered Bacillus coli infections. Jochmann tried 8 normal sera against the Bacillus coli strain from his Case I., and obtained reactions with dilutions no higher than 1 to 40. He thought a reaction with serum diluted 1 to 80 necessary to indicate infection with Bacillus coli, and that the reaction would be of value when no group agglutinins for Bacilli typhosus and paratyphosus were obtained. If the latter were present, one might still obtain a specific Bacillus coli reaction by saturating the sera (by absorption) after Castelanni's method. Later, Jochmann tested the sera of 16 other Bacillus coli infections and obtained reactions with highly (?) diluted serum, so that he disagreed with Köhler and Scheffler, who claimed that such reactions are of no value. Jochmann also concluded that the homologous strain would agglutinate with more highly diluted sera than the heterologous strains, as stated by Pfaundler, which is contrary to the experience of Klieneberger and to our results.

Fehling's article deals mainly with infections of the genito-urinary tract during pregnancy and the puerperium. In one case of pyelo-nephritis in pregnancy, with fever for the fourteen days *ante partum* and at delivery, cultures from the blood were sterile; and cultures from the fœtus were sterile. The fever disappeared on the fourth day of the puerperium, and the bacteruria persisted. Fourteen days after delivery the mother's blood, diluted 1 to 150, agglutinated a bacillus (Bacillus coli) isolated from the urine. He concluded that the Bacillus coli was in the mother's blood at the same time, admitting the possibility of agglutinating substance coming from the fœtus through the placenta. From another case, following an obstetrical operation, he obtained Bacillus coli from the blood, urine, sputum, and sweat, and this case he considered the eighth of pure Bacillus coli sepsis recorded in the literature. No agglutination tests were carried out.

The nosological position to be given to the typhoid-like cases caused by Bacillus coli communis demands brief consideration. As in the case of typhoid-like infections by the intermediate members of the Typhaceæ, it is impossible to differentiate these cases from infections by Bacillus typhosus by clinical methods alone. The assistance of the laboratory is required. Before the development of exact bacteriological diagnosis, all typhoid-like cases, by whatever member of the group they were caused, were considered as typhoid fever. The diagnosis was based necessarily upon clinical data. Since the discovery that the symptom-complex of typhoid fever may be caused by several members of the Typhaceæ, the nosological position of these cases has been under discussion.

Two courses are open to us: to classify the cases clinically or bacteriologically. The former course is the simpler, and is followed in the case of many other diseases. Classification on a bacteriological basis necessitates the introduction of a separate term for each variety of infection. Therefore, we are inclined to advocate the classification of all cases of infection by the Typhaceæ, *when they pursue a typhoid-like course,* as clinical typhoid fever.

Conclusions—1. Isolated reactions against Bacillus coli are without significance in respect to the cause of infection.

2. The blood serum of a case of infection by Bacillus coli communis may contain agglutinins for certain strains of this group while the infection persists and not upon the patient's return to health.

3. The detection of an increment of agglutinins in the blood serum for a particular strain of Bacillus coli cummunis is evidence of a local or general infection with that strain.

4. Some strains of Bacillus coli communis are capable of causing a disease clinically identical with typhoid fever.

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DIET IN TYPHOID FEVER.*

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The conclusions which I have reached concerning the food requirements of the typhoid patient are based on studies on the protein metabolism of the disease which have been carried out in Bellevue Hospital and the Department of Experimental Pathology of Cornell University, in collaboration with Dr. P. A. Shaffer, during the last two years.

I believe that the solution of the essential problems of the typhoid-fever diet will be found in the correct answers to two questions:

I. Shall the typhoid fever patient be given enough food to meet his energy requirements?

II. How much food may be considered necessary to fulfill these requirements?

It is obvious that the digestibility and general suitability of the various foods can not be ignored, and these will be referred to later.

I. Shall the Typhoid Fever Patient be Given Enough Food to Meet His Energy Requirements?

Brief reference to the history of typhoid diets will asist us in finding the answer to this question.

Starvation was the accepted practice for centuries in fevers of all kinds, and included deprivation of water. Graves (1) (1835) convinced himself that, for want of food, the ill effects of starvation were added to the ravages of the disease and recommended a diet which at that time was considered revoluntionary. The diet consisted of carbohydrate-water made from toast-crumbs, meat-broths and jellies. It is difficult to estimate the caloric value of Graves' diet, since exact quantities are not mentioned, but at the most liberal reckoning it furnished not more than 300 calories in 24 hours—the equivalent of about 10 ounces of milk. Graves' belief that patients were benefited by this meager diet was shared by the great Trousseau and other eminent men of his time. The next advance in the feeding of typhoid patients was due, according to Nichols (2), to the teaching of the late Austin Flint. Flint popularized the milk diet (about 1870). The usual quantity of milk taken by a typhoid patient in 24 hours—2 quarts—furnishes about 1,400 calories. The milk diet remained unchallenged until 1892, when Peabody's (3) paper, questioning its suitability, was published. Since 1892 there has grown up a school of practitioners who advocate liberal diets. Among them may be mentioned Shattuck (4), Barrs (5), Bushuyev (6), Fitz (7), Mueller (8), Manges (9), Kinnicutt (10) and Le Fevre (11). Bushuyev is the only one of these authors who has mentioned the quantities of the various foods to be given, and, therefore, the caloric values of these diets are difficult to estimate. Bushuyev's diet furnishes approximately 2,000 calories a day.

Thus, in each of these three diet-periods, there has been an increase in the energy value of the food recommended—an increase of 1,100 calories a day from Graves to Flint and a further increase of 600 calories from Flint to Bushuyev. With each addition to the diet the statement has been made that the patients have been benefited. With respect to each addition, the profession as a whole has been perhaps too conservative.

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Since the chief objections which have been raised to the liberal diets relate rather to the physical state of the food than to the amount of energy they furnish, no attempt will be made at this time to answer them.

The history of diets in typhoid fever, then, clearly indicates a steady, but very slow, tendency to increase the amount of food allowed to the patients. Only exceptionally to-day do we find physicians, once they have used the higher caloric diets, advocating a return to the older methods, and as a rule their arguments are based on questions of digestibility rather than on the energy value of the foods. McCrae (12) has expressed the opinion that more harm may result from overfeeding than from underfeeding, but he is evidently referring to the possibility of setting up digestive disturbances. A distinction must be made between properly nourishing and improperly feeding a patient.

Turning from the history of the typhoid diets and the claims which have been made for them, we may inquire whether there is evidence that definite harm may come to a patient through partial starvation. It is well known that partial starvation lowers the resisting power of healthy persons, and there is reason to believe that immunity to infective diseases is not readily acquired when patients are undernourished. Healthy laboratory animals develop a better immune serum than those which are not robust. Ewing (13) believes that many of the clinical and pathologic phenomena in severe cases of typhoid fever are directly attributable to an autoin-

Fig. 1.—Apparatus for weighing bed patients constructed by hospital carpenter. The height of the table when placed on scales corresponds with that of the bed. The legs of table which just clear the floor prevent tilting.

toxication resulting from the excessive destruction of body tissues. Furthermore, Ewing and Wolf (14) state, in a recent study of the urinary nitrogen in typhoid fever, that "the most obvious conclusion of this study is the inadequacy of the diet used in these cases and of that generally employed in typhoid fever."

There is, therefore, strong experimental and clinical evidence in favor of giving typhoid patients sufficient food to meet their demands for energy.

II. How Much Food May be Considered Necessary to Fulfill These Requirements?

In answering this question I shall consider, first, the energy value of the food. The relative proportions of protein, fat and carbohydrate to be employed will be referrd to later.

One of the chief characteristics of typhoid fever, as we know it, is emaciation (Fig. 1). Losses of 25 pounds during the course of cases of even moderate severity

are not uncommon, and as much as 50 pounds may be lost by patients during prolonged, severe attacks. If these losses concerned only fat and water, they would probably not be serious, but they involve muscle and other tissues as well. Losses of from 15 to 20 gm. of nitrogen a day, representing from ½ to ¾ pound of muscle, are not unusual. Scarcely any one would deny that these losses should be prevented if possible, provided the means taken for their prevention is not more dangerous than the losses themselves. The hunger of many patients during the course of the disease and of all patients during convalescence is probably Nature's protest against the practice of partial starvation. Patients who are well enough complain of it, those who are too ill to complain probably have even greater need for food.

The loss of weight in typhoid fever has been attributed to two causes: to the temperature and to so-called toxic destruction.

Fig. 2.—W. G. Blood culture positive. Very severe. Temperature 103-105° F. Duration of fever 47 days. Relapse of 27 days' duration. Ill for 3 weeks before admission. Said he had lost 15 lbs. Weight on admission, 151 lbs.; at end of first period, 140 lbs.; at beginning of relapse 144 lbs.; at end of relapse 140 lbs.; at first day up 154 lbs.; on discharge, 174 lbs. Picture was taken before patient was allowed out of bed.

The Temperature—The belief is common, even among the laity, that fever burns up tissues. Fritz Voit (15) and Linser and Schmid (16) have shown experimentally both in animals and man that pyrexia does increase metabolism. There is, therefore, a substantial basis for the common belief.

Toxic Destruction—In addition to the febrile loss of body substances, there is a further increase in metabolism in the course of infective diseases which is due to the action of bacterial toxins. This is the so-called toxic destruction. The manner in which the toxins act is not definitely known.

Shaffer and I have found in our cases (17) that the losses due to both of these causes can be prevented by a high caloric carbohydrate diet. As no diet hitherto proposed for typhoid fever has furnished sufficient energy for metabolic exchanges of the patient, we have concluded that the most potent factor in the losses of the disease is partial starvation.

We may calculate the minimum energy requirement of the typhoid patient as follows: A normal man at ordinary rest requires about 33 calories per kilo of body weight each day. According to Krehl (18) the average typhoid patient requires a 25 per cent. addition to this in order to meet the febrile increase in heat production. This gives 41 calories per kilo of body weight per day or approximately 3,000 calories for a man weighing 150 pounds. It must be emphasized that this is the calculated minimum requirement.

If this calculation is approximately correct, then a patient weighing 150 pounds, taking 2 quarts of milk a day, is getting only 50 per cent. of his minimum requirement, and a patient of the same weight on a "liberal diet" is getting only 75 per cent. of this requirement. As a matter of fact, the discrepancies are even greater, since we found that the optimum requirement varied in different patients and at different stages of the disease, but was always greater than the calculated minimum. Our best results were obtained when the diets furnished from 60 to 80 calories per kilo per day, or 4,000 to 5,500 calories. In once case we reached 100 calories per kilo or 6,000 calories a day.

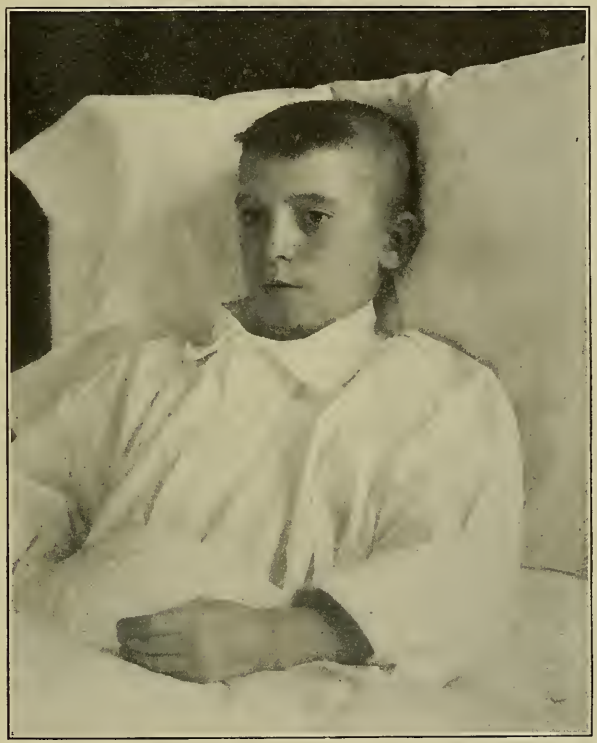

Fig. 3.—J. C. Blood culture positive. Severe. Temperature 101-105° F. Duration of fever 21 days. Weight, 12th day, 60½ lbs. (2 days after admission); 16th day, 58 lbs.; 18th day, 59½ lbs.; 22d day, 59 lbs.; 26th day, 58 lbs.; 28th day, 60 lbs. Picture was taken before patient was allowed out of bed.

We have studied patients on a strict mik diet—2 quarts a day—and found that they lost from 5 to 12 grams of nitrogen. These losses would cease, or at least be greatly reduced when the energy value of the diet was raised. Forty-six patients altogether have been on our diet, with only one death. This was a case of ambulatory typhoid; the patient's pulse was alarmingly feeble on admission to the hospital, and he died a week later from what appeared to be acute dilatation of the heart. (I feel that this case might, with fairness, have been excluded from the total.) Many of the 46 patients suffered from very severe forms of typhoid fever. For example, the temperature ranged from 103 to 105° F. in one case and lasted 47 days, with a relapse of 27 days' duration. Some of the patients were kept almost in nitrogen equilibrium throughout the disease. It was not unusual for patients to weigh as

much or even more when they were allowed to get up (usually about the fourteenth day of convalescence) as when they were taken ill. In one instance the patient actually gained 2 pounds during a sharp relapse of 10 days' duration. In all instances, the patients appeared brighter and stronger and better able to fight the disease. The percentage of relapses was slightly lower than in another division of the hospital where the usual diets were employed. I do not feel disposed to make any statement as yet regarding the course and rapidity of convalescence. All of the patients left the hospital in excellent condition. Some of them I have been able to follow, and the impression I received was that convalescence progressed rapidly. But it is difficult to judge of this unless the patient can be seen frequently, which is manifestly impossible in the case of hospital patients.

Since the calculated minimum requirement of 3,000 calories diminishes but does not prevent protein loss, I would answer the second question by saying that a patient of 150 pounds' weight should be given food equivalent to 4,000 calories a day, but that the greater the energy value of his food, provided his digestive organs can handle it, the greater will be the sparing of protein and other body substances.

Diet—The diet we used consisted, in the main, of milk, cream, milk-sugar and eggs. In addition, we allowed small slices of stale bread or toast, with as much butter as the patient wished. The daily quantities of these articles of food were about 1½ quarts of milk, from 1 to 2 pints of cream, from ½ to 1⅔ pounds of milk-sugar and from 3 to 6 eggs. It will be necessary to say a few words about each of these articles.

Milk: I am convinced, after much experience with it, that milk, in moderate quantity, is not an undesirable constituent of the typhoid diet. When the quantity is excessive, it may unquestionably produce harm, but the argument that it forms an excellent culture medium for the typhoid bacillus in the intestine has been exploded by the investigations which have shown that typhoid fever is a bacillemia. Milk in the quantity mentioned has not produced tympanites in our cases. Occasionally milk curds have appeared in the stools and then the quantity of milk has been diminished or it was peptonized. A good average milk will furnish 740 calories to the quart.

Cream: Though cream furnishes a large amount of energy, it is not advisable, according to our present knowledge, to give more than one-third of the total calories of the diet in the form of fat. Fat in the food, if absorbed, will protect an equivalent amount of fat in the body. Fat protects protein also, but not so efficiently as does carbohydrate Other objections to cream in large amounts are its tendency to upset the stomach and to produce diarrhea. Patients usually can take a pint of cream a day without difficulty. We have given as much as 42 ounces. In only one instance has the cream disagreed. This patient developed diarrhea when the quantity reached a quart a day. The diarrhea stopped immediately when the cream was withdrawn. The cream supplied at Bellevue Hospital contains from 25 to 30 per cent. of fat and furnishes 1,300 calories to the pint.

Milk-sugar: Carbohydrate protects body protein better than any other foodstuff. For this reason a large proportion of the energy of our diet is supplied in that form. Starches can not be used in quantity because of their bulk and the consequent tax on the digestive organs. Therefore, it became necessary to select one of the sugars. We chose milk-sugar because it is not very sweet and not likely to pall on the taste as other sugars, and because it does not so readily produce digestive disturbances. We have not found that it exhibited the laxative properties which have been ascribed to it; in fact, patients taking it often suffered from the constipation which is so common in typhoid fever.

The objections which we have found to milk-sugar are: some patients complain that it is too sweet; in some instances it produced nausea and vomiting, but more often vomiting without nausea, the stomach contents being simply regurgitated. When vomiting occurs, the milk-sugar should be stopped. As a rule, however, its administration may be resumed in smaller quantities after several days and the quantity then be gradually increased. In a few instances the milk-sugar has caused moderate tympanites. We have not had a patient who could not be educated to take it in sufficient amount to materially raise the caloric value of the diet. The method of giving the milk-sugear will be discussed later. Milk-sugar furnishes 4 calories for each gram, or 120 per ounce.

Eggs: While it has not been determined definitely how much nitrogen a typhoid patient requires in 24 hours, our results indicate that the optimum amount lies between 12 and 16 gm. One and one-half quarts of milk and a pint of cream furnish 11 grams of nitrogen and we made up the deficit with eggs. A two-ounce egg supplies 1 + gm. nitrogen.

We chose eggs because they are easily digested and readily obtained. Meat and home-made meat juice are more likely to cause digestive disturbances. I have

specified "home-made" meat juice because the consensus among scientists is that commercial meat preparations possess very little food value (19).

It is important that the protein content of the typhoid diet be kept as low as is consistent with the nitrogen demands of the patient. In addition to digestive disturbances, the injudicious administration of meat may seriously disorder metabolism. It is well known that meat may cause the *febris carnis*. Ewing and Wolf (14) have recently found evidence in the urinary nitrogen to indicate that this "meat-fever" is due to the inability of the patient to digest and metabolize properly some alien proteins. They noted also in their cases this very important fact, that the *febris carnis* was soon followed by albuminuria, which, they suggest, may be the starting point of nephritis. Therefore, the caution may be repeated, to keep the protein content of the typhoid diet low during the disease and to allow meat sparingly early in convalescence.

Some Practical Considerations—The diet which I have outlined is a difficult one to give to patients, on the whole rather more difficult than milk. Intelligent and

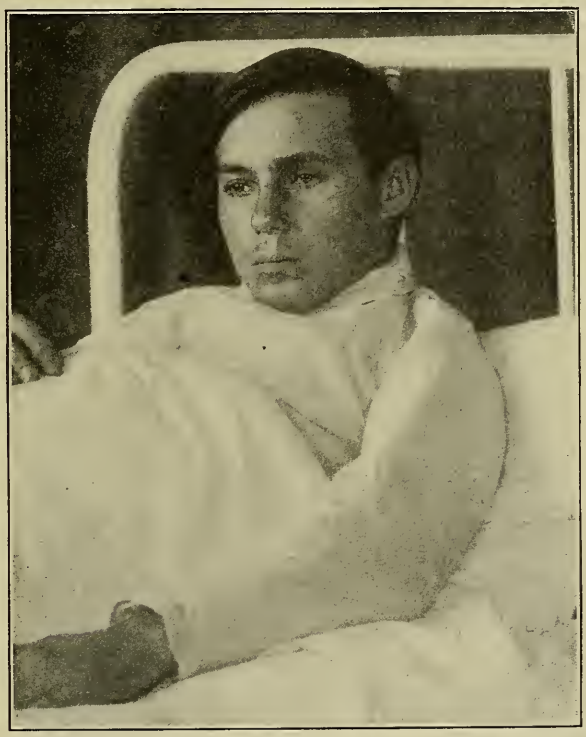

Fig. 4.—P. Z. Blood culture positive. Moderately severe. Temperature 101-103.8 F. Duration of fever 34 days. Weight 6th day, 129 lbs.; 10th day, 132 lbs.; 15th day, 136 lbs.; 17th day, 135 lbs.; 21st day, 133 lbs.; 24th day, 132 lbs.; 27th day, 132 lbs.; 35th day, 130 lbs. Picture was taken before patient was allowed out of bed.

reasonable persons, however, take it readily when the objects of the diet are explained to them. In other instances, patients are not told that the milk differs from what they have been accustomed to taking. The greatest difficulty has been experienced with adolescents who refused to take the diet because patients near them were allowed other food. When I had been convinced that the reason for not taking it was sheer stubbornness, I have insisted on carrying out the order. When I have even suspected that the diet was disagreeing with the patient, I have modified or stopped it, but always have cautiously resumed it (Figs. 2 and 3).

The food has been given at two-hour intervals, except that patients have not been awakened at night. The cream has usually been added to the milk, in the proportion of 2 ounces cream to 6 ounces milk, though a palatable ice-cream may be made with cream and milk-sugar. The milk-sugar should be given in small quantities at first—a tablespoonful to the glass of milk—and gradually increased to 4 table-

spoonfuls. Many patients will take 2 ounces of cream, 6 ounces of milk and 2 ounces of milk-sugar several times a day, but this is a rich combination. At other times the milk-sugar may be given in tea, coffee, or cocoa, or it may be made with an egg into soft or baked custard. A milk-sugar lemonade may be given once or twice a day. If the water and sugar are boiled for two minutes before the lemon juice is added, 4 ounces of milk-sugar may be put into 8 ounces of lemonade. If the lemonade is not sweet enough, a tablespoonful of cane-sugar may be added. The eggs may be given soft boiled, soft poached or shaken up in milk, with or without whiskey.

While I believe that the foods mentioned must form the basis of the ideal diet for typhoid fever, much remains to be done in working out details. The greater the variety and the more palatable the dishes presented to the patient the more content will he be to adhere to the prescribed diet. We have not yet been able to devote much time to the selection of variety in foods and dishes, but this is one of the questions which soon will engage our attention.

Conclusions.

1. The practice of partial starvation, at present followed in the treatment of typhoid fever, is highly detrimental to the patient's welfare.
2. It is not only desirable but necessary that the typhoid patient be given sufficient food to cover his energy expenditures.
3. The amount of food required for this purpose will vary with different patients, but may be estimated approximately on the basis of 40 calories per kilogram of body weight per day.

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PROTEIN METABOLISM IN TYPHOID FEVER.*

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It has long been known that during the febrile reaction to acute infections the katobolism of protein is intensified, resulting in an increased excretion of nitrogenous substances in the urine. This phenomenon is of such constant occurrence that it may properly be considered a characteristic of fever.

Because of this increased katabolism and of the disproportion between the anabolism and katabolism of protein the subject becomes poorer in nitrogenous substances. After the termination of the disease the protein katabolism falls in intensity to or even below the normal limit, the anabolic process becomes more prominent, and during this reverse disproportion between the processes of assimilation and destruction the organism repairs its losses of protein and other substances.

These conditions, fever and convalescence, afford two of the most interesting fields for the investigation of the complicated principles of physiological and pathological nutrition, as has been demonstrated by the numerous papers on these subjects.

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During the past two years we have been engaged in a study of the protein metabolism in typhoid fever. The main object of the investigation was a study of certain aspects of the febrile katabolism of body protein. We hoped to determine to what extent, if at all, the loss of body protein during the disease could be prevented or retarded by different forms of food, and to establish the physiological characters of the diets best suited for this purpose. The experiments to be reported concern chiefly the effect of diets rich in carbohydrate. We have also accumulated much material concerning the quantitative composition of the urine from which we hoped some further knowledge might be obtained of the degree of abnormality in the intermediary metabolism of nitrogenous substances in this disease.

For a critical review of the extensive literature relating to the metabolism in fever and allied subjects the reader is referred to various papers, especially that by Kraus, in von Noorden's "Handbuch der Pathologie des Stoffwechsels." We shall cite in the following pages only a few of the papers having an immediate bearing on our experiments.

The Loss of Body Protein.

The loss of body protein, calculated from the minus balance of nitrogen, is very great in typhoid fever. F. Müller's (1) patient who lost 86.4 gm. of body nitrogen, the equivalent of 2.5 kg. of muscle tissue, in eight days is not very unusual. In an experiment reported by Leyden and Klemperer (2) the subject lost 109.4 gm. of body nitrogen, the equivalent of 3.2 kg. muscle tissue, in twelve days. In neither instance do the figures given represent by any means the total loss of body protein during the whole course of the disease in these patients. The loss for short periods is often relatively much greater, a loss of 15 to 20 gm. nitrogen per day not being very unusual in the early stages of severe attacks in muscular individuals.

This loss of body protein, which apparently occurs during all acute infectious fevers, is due both to an increased destruction and to a decrease in the regenerative processes, both changes serving to intensify the disproportion between the anabolism and katabolism of protein.

The increased katabolism is at present generally believed to be due to at least two fairly distinct causes: to the pyrexia itself and to the action of bacterial toxins on the body cells or fluids, quite apart from the pyrexia. The decrease in the anabolism, the regenerative processes, is largely the result of a lowered or insufficient food-supply; the latter point may be better appreciated after considering the factors involved in the febrile katabolism.

Effect of Simple Pyrexia.

An artificial raising of the body temperature above the normal for some hours results in an increased katabolism of protein. Fritz Voit (3) observed that, if the temperature of a fasting dog was raised to 40 or 41 C., the nitrogen excretion was increased about 37 per cent. This increase was obtained only after maintaining the higher temperature for twelve hours, and Voit concluded that the increase of protein metabolism took place after the greater part of the store of glycogen had been exhausted. Schleich (4), Linser and Schmid (5), and others have performed similar experiments. Schleich found the urea excretion of a man to be noticeably increased on raising the body temperature for several hours by means of hot baths to 39.5 C. Linser and Schmid found an increase of protein metabolism on raising the body temperature of a normal man, as well as of a subject of ichthyosis hystrix, above 39 or 40 C. The last-mentioned investigators believe that a simple pyrexia causes an increase in the protein metabolism only when the temperature is above 39 C. (102 F). It appears, therefore, that the febrile temperature in typhoid fever may be one of the factors which increase the protein metabolism.

The Effect of Toxins.

The human subject of an infectious fever excretes, during the height of the disease, much more nitrogen in his urine than does either a starving man or a man whose body temperature has been raised by artificial means. The same rule holds true for animals experimentally infected with pathogenic organisms or injected with bacterial toxins.

Neither simple pyrexia nor the degree of starvation alone is sufficient to explain the whole of the increase in protein katabolism, and it becomes necessary to seek some further factor which may act in this direction. Most writers call this factor the "toxic" or "toxogenous" destruction, meaning merely the effect of the bacterial toxins on the katabolic processes.

While there seems to be no doubt that the toxins have a distinct part in the cause for the febrile katabolism, the mechanism of this "toxic" action is not known.

One hypothesis is represented by the statement of Krehl (6) that it is "very probable that the agent causing the fever actually destroys the cell proteids in various parts of the body." According to this idea the increase in febrile katabolism involves only protein.

Benedict and Surányi (7), on the other hand, deny the existence of this sort of a toxic destruction, believing that the increased protein katabolism is merely a part of an increase in the total metabolism which Aronsohn (8) believes may be caused by the action of toxins on either enzymes or the nervous mechanism controlling the consumption of food and body materials.

Krehl's view of the toxic destruction appears to be supported by the results of May (9), who studied the total metabolism in fasting rabbits infected with hog cholera and found a marked increase in protein katabolism, but no increase in the consumption of fat; though May concluded from his experiments that the increased protein destruction was chiefly the result of an insufficient carbohydrate supply.

Stähelin (10), on the other hand, working with a dog infected with surra, found an increase in the consumption of fat as well as protein, thus indicating that non-nitrogenous substances also take part in the increase of febrile katabolism.

Partial Starvation.

If a subject does not receive food of a sufficient caloric value to meet the daily energy exchange, his body material is drawn on to supply the deficit. This factor is responsible, in most cases of typhoid fever, for a part of the loss of body protein. The caloric value of the diets now used in the disease is lower than would maintain equilibrium in even a normal subject, with the result that there is not only a decrease in the anabolic processes, but the body tissues or fluids are further drawn on for an additional supply of energy.

The degree of this partial starvation and the amount of the contingent (starvation) loss of body protein is determined both by the food intake and by the total requirement for energy. No satisfactory general estimate of the amount of the latter factor can be made at present; it will vary greatly with different subjects and at different stages of the disease.

It is certain that the energy requirement of such subjects is not lower than the normal (about 33 cal. per kilo [11]), but we cannot predict how much greater it is than the normal in any individual case unless we know the extent of the febrile increase in total katabolism. According to Krehl (12), the febrile increase in heat production varies between 10 per cent. and 60 per cent.; the latter estimate would give a requirement of about 53 cal. per kg.

We have attempted above to outline the factors, so far as they are at present known, which are responsible for the febrile loss of body protein. We have seen that the increased katabolism of body protein is due on the one hand to the febrile temperature of the subject and on the other to the action of bacterial toxins; and that this katabolism may be, and usually is, further increased by an inadequate food-supply and the consequent burning of body material as a source of energy. What are the possibilities of retarding the protein katabolism by dietetic means? It is obvious that the increased katabolism of body materials and the loss of body protein due to simple starvation may be prevented by sufficient food.

And if the view held by Benedict and Surányi, Aronsohn, and in a qualified form by May (13) be true, that the effect of the pyrexia and of the action of toxins is merely an increase in the total katabolism, resulting in a greater demand for energy-producing material, the situation with these factors also becomes one of undernourishment. The body protein, together with fat, is drawn on as in simple starvation to meet the demand for fuel, though in larger amounts on account of the increased heat production. The chief obstacle to this view has been the apparent impossibility of preventing a loss of body nitrogen in a fever subject, even though he be given food of such caloric value as supposedly to cover his energy exchange; and the lack of success in such efforts is, in fact, largely responsible for the conception of a "toxic" destruction of body protein, in the meaning of Krehl. But, according to our experiments, the reason for this lack of success is not that it is impossible to prevent this febrile loss of body protein, as would be the case were Krehl's conception true, but that food of sufficient fuel value and of suitable character has not been used.

Voit, and Linser and Schmid, were able to retard the increased protein katabolism of simple pyrexia by giving additional carbohydrate in the food.

To retard or to prevent the excessive katabolism of body protein due to the action of toxins has been found very difficult; the experiments of Weber (14) are the only ones in which success is clearly shown. This investigator injected extract of glanders bacilli into a sheep and obtained a loss of nitrogen, although the anima' received a diet which had previously maintained nitrogen equilibrium. In a second

experiment, with food equivalent to 73 cal. per kg., the animal gained nitrogen during six days of fever. The gain, however, was less than during the normal periods. He was able, therefore, wholly to prevent a loss of body protein which, with less food, would have been caused both by the pyrexia and by the direct action of the toxins on the protein metabolism.

In a subject of typhoid or other infectious fever it is difficult, and usually impossible, to study the effect singly of partial starvation, pyrexia, or the action of toxins on the protein katabolism, and one must ordinarily be content with determining the combined effect. This is essentially what has been done by Weber, by May with rabbits, and by Püritz (15), and Lyden and Klemperer, with human subjects of typhoid fever.

All these experiments give some indication, it seems to us, that the total protein katabolism in fever, and the loss of body protein, may be influenced by the caloric value of the food. May and Weber drew this conclusion from their experiments, but the principle involved does not appear to have been accepted as generally applicable, and the results of these experiments have had no effect upon the dietetic treatment of febrile conditions in the human subject. Puritz believed the loss of body protein to be less with high protein diets; Leyden and Klemperer, though of the same opinion, conclude that the "toxic" loss of protein cannot be affected by any dietary régime.

There are other reasons for believing that food of high caloric value and especially rich in carbohydrate should be effective in protecting the body protein from excessive destruction in fever. The work of Lusk (16), Sivén (17), Landergren (18), Folin (19), Murlin (20), and others has shown the superior value of carbohydrate in sparing body protein in afebrile conditions.

Fat alone fed to an animal retards the loss of body protein little or not at all, but spares an equivalent quantity of body fat (21).

Protein when alone must be given in extremely large amount before nitrogen equilibrium is obtained, because of the large specific dynamic effect (Rubner) of protein in increasing the total metabolism. Carbohydrate alone, on the other hand, may reduce the amount of nitrogen excreted by 50 per cent. to 70 per cent. of the starvation excretion

Our experiments were undertaken with the hope, based on the considerations stated in the preceding pages, that the total febrile destruction of body protein might be decreased even to normal limits by the addition to the food of large quantities of carbohydrate. It seemed to us probable that carbohydrates might exert the same or similar protecting influence on the body protein during the febrile reaction in man as they do during partial starvation.

These expectations have been realized to the extent that we have found it possible, by giving diets of unusually high caloric value, and consisting principally of carbohydrate, very greatly to diminish and in some instances wholly to prevent the loss of body protein as indicated by the nitrogen balance. Our investigation includes work on twenty-four subjects of typhoid fever, the results from all of which show, with a fair degree of uniformity, though to varying extents, that other factors, such as temperature, intensity of the febrile process, protein intake, etc., being the same or comparable, the loss of body protein becomes less the higher the caloric value of the food. The results from only seven subjects need be given. The results and conclusions from the work with other subjects are in substantial agreement with these.

Plan of Experiments.

The procedure was varied with the different subjects. A constant diet from day to day was frequently impossible, but the amount of food taken in each twenty-four hours was accurately recorded. The protein, fat and carbohydrate, as well as the caloric value of the food, has been calculated from the following data, based in part on our own analyses made from time to time and in part upon König's and Atwater and Bryant's tables.

	Protein. %	Carbohydrate. %	Fat. %
Milk (by volume)	3.3	5.0	5.0
Cream (by volume)	2.0	3.0	30.0
Butter (by weight)	....	....	85.0
Toast	11.0	60.0	....
Eggs (selected to weigh about 60 gm. gross)	12.0	....	9.0
One egg	(7.2 gm.)	....	(5.4 gm.)
Lactose	....	100.0	....
"Somatose"	12.4% nitrogen		
Liebig's meat extract	9.2% nitrogen		
Whisky	40.0% alcohol		

The energy of the diets is calculated on the basis of Rubner's figures:

1 gm. protein.....4.1 cal.
1 gm. carbohydrate.....4.1 cal.
1 gm. fat.....9.3 cal.

Nitrogen × 6.25 = protein.

The urines were collected in twenty-four-hour quantities. The collection of complete twenty-four-hour urines from bed patients who are acutely ill is not an easy task, and in a large and busy ward in a general hospital is frequently very difficult. For the success of an investigation of the nature here reported it is necessary that one have every possible assurance, rather than only an assumption, that the urines are complete. During the last half of the work two special nurses, who had no other duties than attendance on the patients being studied, were detailed through the courtesy of Dr. S. T. Armstrong, superintendent of the hospital, and of Miss Goodrich, superintendent of nurses. To the care of these nurses is due the infrequency of the loss or urines as well as the successful and accurate administration of the food.

The following is a form of printed blanks which were written up and signed by the nurses and sent to the laboratory with each bottle of urine or feces:

METABOLISM IN FEVERS.

Name ..... Ward ..... Bed .....

Urine for 24 hours, ending at..... a. m. p. m. (date).....

Feces for.....days, from..... a. m. p. m. .....to..... a. m. p. m. .....

Temperature: lowest.....at..... a. m. p. m. .....; highest.....at..... a. m. p. m.

Weight of patient.....lbs. at..... p. m. a. m. (date).....

NURSES: ..... | Quantity of Urine.

Each nurse, when she goes off duty, will please sign her name above, stating the time she was in charge of the patient. If no accidents concerning the administration of food (as refusal to take all or part, or loss of through vomiting—if patient vomits, state hour) or the collection of the *complete excreta* have occurred, she should write O. K. after her name. Otherwise, she should describe on the back of this sheet the amount of food refused or left or vomited, and the approximate quantity of urine or feces lost and how it was lost. Please send this sheet to the laboratory with its corresponding specimen.

When this sheet is used for a specimen of feces, data concerning urine, temperature and weight may be omitted.

By this means responsibility for the collection of excreta and administration of food was centered on individuals, with the result that accidents of this nature were rare, and, more important still, were accurately recorded when they did occur (22).

The urines were analyzed at once for total nitrogen, kreatinin, kreatin, and in many instances for other substances. In some cases "composites" representing a number of days, were made by mixing aliquot parts of consecutive urines. These composites were then analyzed for the substances stated in the tables.

The feces, marked off by charcoal, were collected and analyzed for total nitrogen during a part of some experiments, but not in all. It is to be regretted that the limited capacity of the laboratory prevented further work on the feces. For the calculation of the nitrogen balance we have used nitrogen figures for each day's urine, and, except where the feces were analyzed, have arbitrarily taken 15 per cent. of the food nitrogen as representing the amount of nitrogen in the feces.

This latter assumption is admittedly a source of error, but this error is probably fairly constant with individual patients and, we believe, does not affect the validity of our conclusions, based as they are on comparative figures (23).

The analytical methods used were:

Kjeldahl method for total nitrogen; Folin's method for urea, kreatinin, kreatin, total sulphur (24) and its partition among inorganic, ethereal and neutral sulphur, titrated acidity (25) and indican (26); Boussingault-Shaffer method for ammonia (27); Folin-Shaffer method for uric acid; Salkowski method for xanthin bases; Volhard method for chlorids; Fehling's or Pavy's methods for sugar; Shaffer's method for beta-oxybutyric acid (28), and a modified Messinger-Huppert method (28) for acetone plus diacetic acid. The fraction called "rest" nitrogen is the difference between the total nitrogen of the urine and the sum of urea-, ammonia-, kreatinin-, kreatin- and uric-acid nitrogen.

Detail of Experiments.

Patient 1—R—n, male, 23 years of age, fairly well nourished, admitted the seventh day of the disease. Positive serum reaction. Illness severe. Duration of the fever thirty-five days. Two recrudescences.

Table 1.—Patient 1, R—N: Temperature and Food.

Day of Disease.	Temp., F.		Food.						
	High.	Low.	Milk c.c.	Cream c.c.	Lactose Gm.	Eggs.	Protein.	Fat.	C.H.
			Period I.						
12	104.8	103.0	1200	95	460	2	60.0	99	523
13	104.0	102.0	1080	120	610	2	52.5	101	668
14	104.4	101.0	1200	60	515	2	55.0	89	577
15	104.0	101.4	1470	....	450	2	63.0	84	523
16	103.0	101.6	1000	60	365	2	48.6	79	417
17	102.6	100.6	990	120	420	2	49.5	86	473
18	102.6	99.0	1200	150	455	2	57.0	116	520
19	103.6	100.0	1290	150	510	2	60.0	120	579
Average							55.7	97	535
			Period II.						
20	104.4	101.0	1380	150	500	3	70.0	130	574
21	102.0	98.0	1200	180	500	3	64.8	130	565
22	102.8	98.4	1260	150	480	3	65.2	124	547
23	102.6	98.4	1200	270	500	4	74.2	132	565
24	102.6	99.0	1200	300	505	3	67.0	166	574
25	102.0	99.0	960	300	510	2	52.0	149	567
Average (omitting last day)							68.2	136	565
			Period III.						
26	102.4	99.2	240	420	515	1	23.3	143	540
27	103.6	100.6	....	540	520	..	10.8	162	536
28	104.8	99.6	....	600	515	..	12.0	180	533
29	102.8	101.6	....	630	475	..	12.6	189	494
Average							15.4	162	536
			Period IV.						
30	102.2	99.0	2400	....	....	..	79.2	120	120
31	100.6	99.0	2400	....	....	..	79.2	120	120
32	104.6	101.0	2400	....	....	..	79.2	120	120
33	101.0	99.6	2400	....	....	..	79.2	120	120
34	102.0	99.0	2400	....	...	..	79.2	120	120
35	100.2	98.4	2160	....	....	..	71.5	108	108
Average (omitting last day)							79.2	120	120
			Period V.						
Convalescence.									
1	99.0	98.0	1200	270	357	2	59.4	152	425
2	98.4	97.0	1440	210	500	3	73.3	151	578
3	99.0	97.6	1440	210	500	4	80.5	156	578
4	99.4	97.2	1440	240	505	5	88.3	171	584
5	100.0	99.0	1410	240	510	4	80.0	164	588
6	99.6	98.4	1500	240	510	5	90.3	174	592
7	99.6	99.0	1560	150	485	5	90.5	150	567
8	99.0	98.0	1620	330	395	5	96.0	207	485
Average (omitting first day)							85.0	167	564

Table 2.—Patient 1, R—N: Daily Nitrogen Balance.

Day of Disease.	Calories.		C. H. Cal. Per Kg.	Nitrogen Balance.		
	Total.	Per Kg.		Intake.	Excretion.*	Balance.
			Period I.			
12	3310	61	40	9.6	14.3	—4.7
13	3890	70	51	8.4	10.8	—2.4
14	3430	63	44	8.8	13.8	—5.0
15	3180	59	40	10.1	14.8	—4.7
16	2645	49	32	7.8	15.0	—7.2
17	2940	54	36	7.9	15.7	—7.8
18	3440	64	39	9.1	16.0	—6.9
19	3735	69	44	9.6	11.4	—1.8

Day of Disease.	Calories. Total.	Calories. Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance. Intake.	Excretion.*	Balance.
		Period II.				
20	3850	71	43	11.2	11.9	—0.7
21	3790	70	43	10.4	10.9	—0.5
22	3660	68	41	10.4	9.7	+0.7
23	3850	71	43	11.9	8.9	+3.0
24	4170	77	43	10.7	8.7	+2.0
25	3920	73	43	8.3	8.8	—0.5
		Period III.				
26	3640	67	41	3.7	7.0	—3.3
27	3750	70	41	1.7	5.1	—3.4
28	3900	72	40	1.9	5.8	—3.9
29	3840	71	38	2.0	....	....
		Period IV.				
30	1928	36	9	12.7	11.3	....
31	1928	36	9	12.7	16.6	—3.9
32	1928	36	9	12.7	16.3	—3.6
33	1928	36	9	12.7	15.0	—2.3
34	1928	36	9	12.7	15.5	—2.8
35	1740	..	...	....	....	....
Convalescence.		Period V.				
1	3390	63	32	9.5	11.0	—1.5
2	4070	75	43	11.7	10.3	+1.4
3	4150	77	43	12.9	9.3	+3.6
4	4340	80	44	14.1	....	....
5	4260	79	44	12.8	10.3	+2.5
6	4420	82	45	14.4	10.3	+4.1
7	4090	76	43	14.5	10.5	+4.0
8	4300	80	37	15.3	12.2	+3.1

* "Excretion"=Total nitrogen of urine + 15 per cent. of food nitrogen.
Weight on twenty-seventh day of disease, 54 Kg.

TABLE 3.—PATIENT 1, R—N: DAILY ANALYSES OF URINE.

Day of Disease.	Urine. Volume c.c.	Gm. Nitrogen. Total.	Kreatinin.	Kreatin.	Rest.*	Per Cent. of Total Nitrogen. Urea+NH_3.	Rest.*
			Period I.				
12	700	12.9	0.54	0.08	1.62	82.8	12.5
13	600	9.5	0.44	0.10	1.52	78.4	16.0
14	800	12.5	0.58	0.09	1.19	85.1	9.5
15	900	13.3	0.60	....	1.70	82.6	12.8
16	960	13.8	0.54	0.21	1.23	84.7	8.9
17	980	14.5	0.54	0.28	1.56	83.6	10.8
18	1580	14.6	0.54	0.42	1.37	84.3	9.4
19	940	10.0	0.53	0.29	0.73	84.7	7.3
			Period II.				
20	1180	10.2	0.54	0.25	0.94	83.0	9.2
21	1170	9.3	0.50	0.03	0.84	85.3	9.0
22	1120	8.1	0.44	0.03	0.81	84.3	10.0
23	840	7.1	0.40	0.03	1.01	79.7	14.3
24	810	7.1	0.35	0.00	1.38	75.7	19.4
25	930	7.6	0.47	0.00	1.17	78.5	15.4
			Period III.				
26	975	6.4	0.40	0.00	1.10	76.5	17.3
27	1140	4.8	0.42	0.00	0.55	79.5	11.5
28	900	5.5	0.55	0.05	0.95	71.8	17.4
29	Urine lost.						
			Period IV.				
30	1450	9.4	0.50	0.00	....	....	....
31	1560	14.7	0.62	....	....	....	....
32	1280	14.4	0.52	0.09	....	....	....
33	1560	13.1	0.47	....	....	....	....
34	970	13.6	0.49	....	....	....	....
35	Urine lost.						
Day of Convalescence.			Period V.				
1	910	9.6	0.32	....	....	....	....
2	950	8.6	0.39	....	....	....	....
3	780	7.4	0.39	....	....	....	....
4	Urine lost.						
5	1100	8.4	0.49	....	....	....	....
6	1080	8.2	0.45	....	....	....	....
7	940	8.3	0.35	....	....	....	....
8	1160	9.9	0.41	....	....	....	....

* "Rest" includes uric-acid-nitrogen.

TABLE 4.—PATIENT 1, R—N: AVERAGES FROM PERIODS.
Figures given for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food. Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion N.	Balance N.	Urine. Kreatinin N.	Kreatin N.	"Rest" N. Gm.	Per Cent. Total N.	Kreatinin Coef.
					Period I.							
8.....	104.8–102.6	62	16	41	8.9	13.9	—5.0	0.54	0.21	1.49	11.8	10.0
					Period II.*							
5.....	104.4–102.0	71	23	43	10.9	10.0	+0.9	0.45	0.02	1.02	12.2	8.3
					Period III.							
3.....	104.8–102.4	70	28	41	2.4	5.9	—3.5	0.46	0.02	0.87	15.6	8.5
					Period IV.†							
4.....	104.6–100.6	36	21	9	12.7	15.8	—3.1	0.52	0.09‡	....	....	9.6
					Period V.†							
6.....	Normal	77	29	43	13.6	10.5	+3.1	0.41	....	....	....	7.6

* Last day of period omitted from average.
† First day of period omitted from average.
‡ Result of third day of period.

The experiment began on the twelfth day of the disease and continued thirty-two days, during the last eight of which the temperature was normal.

With the exception of six days, when a strict milk diet was given, the patient received food of high caloric value; and during four days the protein intake was kept very low, maintaining at the same time the high caloric value of the food. The detailed results of this experiment are given in Tables 1, 2 and 3. Throughout the whole experiment there is a fairly close relation between the nitrogen balance and the caloric and protein value of the food.

This experiment may be conveniently divided into five periods, the average results of which are given in Table 4, to which the attention of the reader is particularly directed.

During the first period of eight days (twelfth to nineteenth days of disease) when receiving food equivalent to 62 calories per kg. and 8.9 gm. of nitrogen, the patient *lost an average of 5 gm. of body nitrogen each day.* This is just the type of result which led von Leyden and Klemperer and others to conclude that the harmful effect of the toxins in causing a destruction of body protein cannot be prevented. But, as we shall see, the loss during this period was undoubtedly much less than would have occurred with food of a lower caloric value. In the second period, when the temperature was still fairly high, and the fever process certainly still active, the food was further increased to 71 calories per kg. and 10.9 gm. of nitrogen, with the result that the subject *gained an average of* 0.9 *gm. nitrogen each day!* Although the nitrogen intake was increased by 2 gm., the excretion was decreased by 3.9 gm. It is clear that during this period the whole of the febrile increase in protein katabolism was either prevented by the large food supply, or was more than compensated for by a retention of food protein.

In interpreting an experiment of this sort we must, of course, remember that the condition of the subject or the intensity of the febrile process is constantly changing, and we must so far as possible make allowance for this factor. The difference between the nitrogen balance of Periods I and II is undoubtedly due in part to such a change in the intensity of the processes involved. On the other hand, we certainly have no reason for believing that the febrile katabolism, including the action of the toxins, had ceased during Period II, and, if this action was still at work, we can scarcely avoid the conclusion that the loss of body protein which would otherwise have taken place was prevented by the high caloric value of the food. In Period I the katabolism was more intense, the demands were greater than the supply, and the subject lost body protein; in Period II the katabolism was less intense, the food supply was greater than the demand, and the subject gained protein.

In Period IV, the last of fever, pathologic katabolism was still taking place. The food contained more protein (12.7 gm. nitrogen), but equaled only 36 cal. per kg. and the subject lost 3.1 gm. nitrogen per day. In the absence of any increased katabolism, this food should maintain equilibrium. In Period VI, the first six days of normal temperature, the food was again increased to 77 cal. per kg. and the subject gained 3.1 gm. nitrogen per day.

Period III is of interest as showing the importance of at least a moderate amount of protein in the food. The fat and carbohydrate intake was kept practically the same as in Period II, which gave a plus balance of 0.9 gm. nitrogen, but the protein was decreased to a very small amount (average 2.4 gm.) with the result that the patient lost 3.5 gm. nitrogen per day. This loss, however, seems remarkably small under the circumstances; the nitrogen excretion was reduced to 5.9 gm.

It should be noted that the marked sparing of body protein observed during this experiment was accomplished by food very rich in carbohydrate. In four periods the subject received each day carbohydrate equivalent to more than 40 cal. per kg.

The kreatin excretion of this subject is also significant. We shall have frequent occasions to refer to the excretion of kreatin and the following explanation of the bearing of this substance may be stated at this point. Endogenous kreatin is not excreted under normal conditions, but, as has been shown (29), kreatin is excreted when muscle tissues are being broken down or absorbed. One of the most marked instances of a large excretion of kreatin is in women during the first week postpartum, when, as is known, the involution of the muscular wall of the uterus is proceeding most rapidly. The nitrogen derived from this absorbed protein is excreted at the same time in the urine, resulting in a marked minus balance (30). This relation is also shown in dogs by the experiments of Murlin (31).

If, as seems probable to us, the belief is correct that endogenous kreatin is excreted only when protein of muscle tissue is being katabolized, it should be possible to determine from the amount of kreatin excreted approximately the extent of the abnormal destruction or consumption of muscle tissues. While recognizing that this

conception has not been definitely proved, it appears sufficiently clear to justify its use in the interpretation of our results.

The amount of kreatin excreted in Period I very nearly corresponds with the loss of nitrogen, indicating that the body nitrogen lost was in this period wholly derived from muscles; 0.21 gm. kreatin-nitrogen = 0.65 gm. kreatin. Human muscle contains about 0.4 per cent. kreatin; then 0.65 gm. kreatin = 163 gm. muscle, which (× 3.4 per cent. nitrogen) equals 5.55 gm. nitrogen. The sudden drop of kreatin on the second day of Period II (Table 3) from 0.25 to 0.03 nitrogen probably indicates a sudden and marked diminution in the pathologic metabolism of muscle protein; whether as a result of the increased food-supply or of a change in the patient's condition it is difficult to decide. Perhaps both are responsible. In the third period, although there was a loss of nitrogen, kreatin was excreted on only one day, indicating that the nitrogen lost was not directly derived from muscle tissues.

During Period IV kreatin unfortunately was determined on only two days, the result on the third day (0.09 gm. nitrogen) being equivalent to about 2.4 gm. muscle-protein-nitrogen. Accepting this day as representative of the period, the kreatin indicates that the greater part of the protein lost was derived from muscle, in which we may suppose the katabolism to have been increased as a result of the decrease in fuel value of the food.

Patient 2—U—h, male, 24 years of age, laborer, well nourished and of good development, admitted on the tenth day of disease. Blood culture positive. Illness severe. Duration of fever thirty-five days.

The experiment began on the tenth day of the disease and ran for thirty days, during the last eight of which the temperature was normal. This experiment may also be divided into five periods, the average results of which are given in Table 8. The detailed results are given in Tables 5, 6 and 7.

With this subject we see again the marked sparing of the body protein by food rich in carbohydrate, though nitrogen equilibrium was not attained during the fever. In the first period the food contained 9.7 gm. nitrogen and was equivalent to 31 cal. per kg., which fairly represents the diet commonly used in typhoid fever. The patient lost 8.9 gm. of nitrogen each day, and excreted an average of 0.18 gm. kreatin-nitrogen, the latter corresponding to about 4.7 gm. of muscle-protein-nitrogen, and indicating that about half of the nitrogen loss was directly derived from muscle tissue.

In the second period with the temperature fairly high (third week of the disease) the food was increased to 63 cal. per kg., 43 of which were given as carbohydrate. The loss of nitrogen was decreased 5 gm. and the kreatin almost disappeared, the latter, we think, indicating that the pathologic katabolism of muscle protein was practically stopped.

During the third period the diet was again reduced in fuel value to 31 calories per kg., while the protein intake was somewhat increased. The temperature was lower than in the previous periods, but the loss of nitrogen was very considerably increased. Both kreatin and uric acid were slightly higher than in the second period, indicating an increase in the protein katabolism taking place in he muscles. The amount of kreatin excreted was, however, equivalent to only 1 gm. of muscle-protein-nitrogen, or one-seventh of the amount of the minus balance. The greater part of the nitrogen lost was, therefore, probably derived from the blood or tissue fluids.

The food in the fourth period, the last six days of fever, was again of high caloric value, 66 calories per kg., and the subject was almost in nitrogen equilibrium. The kreatin excreted was about the same as during the preceding period, and just about corresponds to the amount of the minus balance (0.7 gm.) of nitrogen, assuming the latter to have been derived wholly from muscle-protein.

The fifth period consists of seven days of convalescence, during which the food was about the same as during Period IV, except for a slight increase in protein. The subject showed a plus balance of 2.5 gm. nitrogen per day. The small amount of kreatin excreted probably indicates that muscle protein was still being absorbed in very slight degree though the loss of nitrogen from his muscle protein is more than compensated for by the retention of food nitrogen.

The experiment shows that the addition to the food of carbohydrate equivalent to 32 calories per kg. was followed by a decrease in the nitrogen loss of 5 gm., and the subsequent withdrawal of this carbohydrate resulted in an increase of 3 gm. in the nitrogen loss. On again increasing the carbohydrate intake to 43 carbohyrate calories per kg. the subject lost an average of only 0.7 gm. of nitrogen during the last six days of fever and gained 2.5 gm. (average) during the first seven days of normal temperature.

Patient 3—Z—o, male, 20 years of age, laborer, well nourished, admitted the fourth day of the disease. Blood culture positive. Illness moderately severe. Sputum

blood-stained but no tubercle bacilli could be found, nor any signs of tuberculosis in the lungs.

The experiment began on the ninth day of the disease and continued for thirty-two days, on the last seven of which the temperature was normal. In this experiment, which is divided into six periods, the total nitrogen, kreatinin and kreatin were

Table 5.—Patient 2, U—H: Temperature and Food.

Day of Disease.	Wt. Kg.	Temp., F. High.	Temp., F. Low.	Food. Milk c.c.	Cream c.c.	Lactose Gm.	Eggs.	Protein Gm.	Fat Gm.	C. H. Gm.
				Period I.						
10	....	104.0	103.0	540	220	180	5	58.0	120	214
11	....	104.0	102.4	600	150	130	3	44.4	91	204
12	....	104.0	102.2	600	225	120	4	50.0	119	157
13	60?	103.5	101.4	2070	....	....	..	68.3	104	104
14	....	103.4	101.6	2160	....	....	..	71.3	108	108
15	....	103.4	101.0	2160	....	....	..	71.3	108	108
Average								60.5	108	149
				Period II.						
16	....	103.4	101.0	1200	120	310	6	85.2	128	374
17	....	103.2	100.0	960	120	480	2	48.4	95	532
18	58?	103.0	101.0	1170	45	540	2	54.0	83	600
19	....	103.4	100.0	1200	120	540	2	56.4	107	604
20	....	103.4	100.0	1200	120	540	2	56.4	107	604
Average (excluding 16th day)								53.8	98	585
				Period III.						
21	....	103.2	100.8	2160	....	....	..	71.3	108	108
22	....	102.4	99.6	2160	....	....	..	71.3	108	108
23	56?	101.0	99.4	2160	....	....	..	71.3	108	108
24	....	101.0	99.2	2160	....	....	..	71.3	108	108
Average								71.3	108	108
				Period IV.						
25	....	102.0	98.0	1140	120	480	2	54.4	104	540
26	....	102.0	99.4	975	120	485	2	49.0	95	537
27	56?	101.0	98.4	990	150	550	2	50.0	105	603
28	....	101.0	98.0	1200	180	550	2	57.6	125	615
29	....	101.0	98.4	1200	240	500	2	58.8	143	567
30	....	100.4	98.4	1200	150	540	2	57.0	116	604
Average (excluding 25th day)								54.5	117	585
Convalescence.				Period V.						
1	....	99.0	98.0	1170	180	490	2	56.6	123	553
2	....	99.2	98.0	1290	150	515	2.5	63.0	123	584
3	55.0	98.8	98.2	1110	270	500	3	63.6	152	563
4	....	99.2	98.2	1230	300	455	3	68.0	167	525
5	....	99.2	98.2	1200	300	490	3	67.0	166	559
6	55.5	99.0	98.2	1230	240	515	2	59.7	145	584
7	....	98.8	98.4	1140	240	515	3	64.0	145	579
8	....	98.8	98.2	1200	180	500	2	57.8	125	565
Average								63.0	146	566

Table 6.—Patient 2, U—H: Daily Nitrogen Balance.

Day of Disease.	Food. Total Calories.	Cal. Per Kg. Total.	Cal. Per Kg. Fat.	Cal. Per Kg. C. H.	Nitrogen Gm.	Excretion* N Gm.	Balance N Gm.
	Period I.						
10	2230	37	19	15	9.3	20.8	—11.5
11	1860	31	14	14	7.1	....	.....
12	1960	33	19	11	8.0	16.3	— 8.3
13	1670	28	16	7	10.9	20.2	— 9.3
14	1730	29	17	7	11.4	17.9	— 6.5
15	1730	29	17	7	11.4	17.9	— 6.5

Day of Disease.	Food. Total Calories.	Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion* N Gm.	Balance N Gm.
		Period II.					
16	3070	53	20	26	13.6	19.3	— 5.7
17	2360	56	15	38	7.8	14.2	— 6.4
18	3450	59	13	42	8.6	13.3	— 4.7
19	3710	64	17	43	9.0	11.6	— 2.6
20	3710	64	17	43	9.0	11.2	— 2.2
		Period III.					
21	1740	31	18	8	11.4	18.0	— 6.6
22	1740	31	18	8	11.4	19.6	— 8.2
23	1740	31	18	8	11.4	18.0	— 6.6
24	1740	31	18	8	11.4	18.0	— 6.6
		Period IV.					
25	3410	61	17	40	8.7	14.3	— 5.6
26	3280	59	16	39	7.8	11.2	— 3.4
27	3650	65	17	44	8.0	8.7	— 0.7
28	3920	70	21	45	9.2	9.5	— 0.3
29	3900	70	24	42	9.4	9.5	+ 0.1
30	3780	68	19	44	9.1	8.4	+ 0.7
Day of Convalescence.		Period V.					
1	3640	66	21	41	9.0	....	.....
2	3790	69	21	43	10.1	8.5	+ 1.6
3	3980	72	25	42	10.2	8.8	+ 1.4
4	3980	72	25	39	10.9	8.1	+ 2.8
5	4100	74	25	41	10.7	6.7	+ 3.0
6	3970	72	24	43	9.5	6.9	+ 2.6
7	3980	72	24	43	10.2	6.5	+ 3.7
8	3720	67	21	42	9.3	7.4	+ 1.9

* "Excretion." — Total nitrogen of urine. + 15 per cent. of food nitrogen.

TABLE 7.—PATIENT 2, U—H: DAILY ANALYSES OF URINE.

Day of Disease.	Urine. Volume c.c.	Gm. Nitrogen as Total.	NH_3.	Kreatinin.	Kreatin.	Uric Acid.	Rest.	Urea.	Per Cent. of Total Nitrogen. NH_3.	Rest.
				Period I.						
10	920	19.4	1.45	0.74	0.27	0.15	1.29	80.0	7.5	6.6
11	Urine lost.									
12	800	15.1	1.38	0.60	0.07	0.12	1.27	77.4	9.1	8.5
13	1400	18.6	1.77	0.66	0.13	0.14	1.04	79.9	9.5	5.6
14	860	16.2	1.37	0.58	0.17	0.13	0.99	80.1	8.5	6.1
15	880	16.2	1.39	0.64	0.26	0.13	0.93	79.4	8.6	5.7
				Period II.						
16	820	17.3	1.51	0.63	0.05	0.13	1.91	75.6	8.8	11.0
17	660	13.0	0.97	0.54	0.04	0.11	1.11	78.7	7.5	8.6
18	760	12.0	1.10	0.56	0.00	0.11	1.00	77.0	9.1	8.3
19	540	10.3	....	0.55	....	....	....	....	....	....
20	670	9.9	0.88	0.54	0.00	0.09	0.64	77.1	8.9	6.5
				Period III.						
21	1360	16.3	....	0.56	0.00?	....	1.29	....	....	8.0
22	1390	17.9	0.94	0.53	0.08	0.12	0.90	85.8	5.2	5.0
23	1500	16.3	0.82	0.48	0.02	0.12	0.76	86.5	5.0	4.7
24	1400	16.3	0.79	0.54	0.03	0.12	0.87	85.6	4.9	5.4
				Period IV.						
25	1130	13.0	0.63	0.53	0.05	0.10	0.83	83.6	4.9	6.4
26	1020	10.0	0.57	0.50	0.03	0.09	0.83	79.8	5.7	8.3
27	900	7.5	0.50	0.40	0.03	0.07	0.60	78.8	6.7	9.3
28	1240	8.1	0.56	0.47	0.00	0.07	0.50	80.5	6.8	6.1
29	1120	8.1	0.57	0.47	0.05	0.04	0.68	77.6	7.0	8.4
30	1350	7.0	0.52	0.45	0.03	0.05	0.52	77.6	7.4	7.4
Day of Convalescence:	1, urine lost.			Period V.						
2	1060	7.0	0.45	0.40	....	0.05	0.72	77.1	6.4	10.2
3	1260	7.3	0.46	0.45	....	0.03	0.45	81.0	6.3	6.2
4	1080	6.5	0.38	0.39	0.05	0.03	0.51	79.1	5.8	7.9
5	1040	5.1	0.37	0.31	0.00	0.03	0.63	73.7	7.3	12.4
6	1440	5.5	0.44	0.40	....	0.03	0.77	69.9	8.0	14.1
7	850	5.0	0.38	0.39	0.00	0.04	0.43	75.5	7.5	8.6
8	940	6.0	0.45	0.41	0.01	0.04	0.64	74.3	7.5	10.7

TABLE 8.—PATIENT 2, U—H: AVERAGES FROM PERIODS.
Figures given for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food. Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion N.	Balance N.	Urine. Kreatinin N.	Kreatin N.	Uric Acid N.	"Rest" N. Gm.	"Rest" N. Total N.	Kreatinin Coef.
					Period I.								
6	104.0–103.4	31	17	10	9.7	18.6	— 8.9	0.64	0.18	0.13	1.10	6.4	10.6
					Period II.*								
5	103.4–103.0	61	16	41	8.6	12.6	— 4.0	0.55	0.01	0.10	0.64	8.1	9.5
					Period III.								
4	103.2–101.0	31	18	8	11.4	18.4	— 7.0	0.52	0.04	0.12	0.95	5.7	9.3
					Period IV.*								
6	102.0–100.4	66	19	43	8.7	9.4	— 0.7	0.47	0.03	0.07	0.72	8.8	8.4
					Period V.*								
7	Normal	71	24	42	10.1	7.6	+ 2.5	0.39	0.01	0.03	0.59	9.7	7.0

* First day of period omitted from average.

TABLE 9.—PATIENT 3, Z—O: TEMPERATURE AND FOOD.

Day of Disease.	Wt. Kg.	Temp., F. High.	Temp., F. Low.	Food. Milk c.c.	Cream c.c.	Lactose Gm.	Eggs.	Protein Gm.	Fat Gm.	C. H. Gm.
				Period I.						
9	....	104.0	102.4	1950	....	590	3	86.0	113	687
10	60.0	103.6	102.0	2000	....	600	3	87.6	116	700
11	....	103.2	101.6	2000	....	600	3	87.6	116	700
12	....	103.2	101.0	2000	....	600	3	87.6	116	700
Average								87.2	115	697
				Period II.						
13	60.6	103.6	101.4	2000	300	600	3	93.6	206	709
14	....	103.2	101.2	2000	300	600	3	93.6	206	709
15	....	102.8	101.0	2000	300	600	3	93.6	206	709
16	61.6	103.2	104.4	2000	300	600	3	93.6	206	709
17	61.3	103.6	101.2	2000	300	600	3	93.6	206	709
18	....	103.6	101.0	2000	300	600	3	93.6	206	709
Average								93.6	206	709
				Period III.						
19	....	103.6	101.0	2000	300	....	3	93.6	206	109
20	....	103.6	100.6	2000	300	....	3	93.6	206	109
21	60.4	103.8	100.4	2000	300	....	3	93.6	206	109
22	....	103.4	100.2	2000	300	....	3	93.6	206	109
Average								93.6	206	109
				Period IV.						
23	....	103.6	99.8	2000	300	670	3	93.6	206	779
24	....	103.4	100.4	2000	300	700	3	93.6	206	809
25	60.0	103.8	99.8	2000	300	750	3	93.6	206	859
26	....	104.8	100.4	2000	300	680	3	93.6	206	789
27	60.0	102.6	100.6	2000	300	690	3	93.6	206	799
28	....	101.8	99.8	1800	270	600	3	86.5	187	695
29	....	101.4	99.2	1800	270	600	3	86.5	187	695
30	....	101.6	99.4	1800	270	600	3	86.5	187	695
Average (excluding first day)								90.6	198	763
				Period V.						
31	59.5	100.8	99.2	1800	270	600	3	86.5	187	695
32	....	100.4	98.6	1800	270	660	3	86.5	187	755
33	....	100.4	98.2	1800	270	660	3	86.5	187	755
Convalescence.										
1	....	99.4	98.4	1800	270	660	3	86.5	187	755
2	....	99.8	98.4	1800	270	660	3	86.5	187	755
3	....	99.6	97.8	1800	270	420	3	86.5	187	515
Average								86.5	187	705
				Period VI.						
4	....	99.6	98.0	1800	270	....	3	86.5	187	98
5	....	99.6	98.0	1800	270	....	3	86.5	187	98
6	....	99.4	97.8	1800	270	....	3	86.5	187	98
7	....	99.2	97.6	1600	240	....	3	79.2	168	87
Average								84.7	182	95

TABLE 10.—PATIENT 3, Z—O: DAILY NITROGEN BALANCE AND URINE.
During Periods III., XIII. and XIV., the food contained "somatose."

Day of Disease.	Calories. Total.	Calories. Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance. Intake Gm.	Excretion* Gm.	Balance.	Urine. Volume c.c.	Nitrogen. Total.	Kreatinin.	Kreatin.
				Period I.						
9	4220	70	47	13.7	15.8	— 2.1	780	13.8	0.67	0.02
10	4330	72	48	14.0	13.1	+ 0.9	640	11.0	0.59	0.03
11	4330	72	48	14.0	15.8	— 1.8	840	13.7	0.59	0.11
12	4330	72	48	14.0	14.5	— 0.5	1140	12.4	0.65	0.05

Day of Disease.	Calories. Total.	Per Kg.	C. H. Cal. Intake Per Kg.	Nitrogen Balance. Excretion* Gm.	Gm.	Balance.	Urine. Volume c.c.	Nitrogen. Total.	Kreatinin.	Kreatin.
				Period II.						
13.....	5200	85	48	15.0	15.2	— 0.2	1210	13.0	0.65	0.00
14.....	5200	85	48	15.0	....	.....	....	....	....	....
15.....	5200	85	48	15.0	14.7	+ 0.3	1220	12.5	0.52	0.02
16.....	5200	85	48	15.0	14.0	+ 1.0	1260	11.8	0.55	0.04
17.....	5200	85	48	15.0	14.9	+ 0.1	1210	12.7	0.53	0.03
18.....	5200	85	48	15.0	16.6	— 1.6	1660	14.4	0.58	0.02
				Period III.						
19.....	2750	45	7	15.0	21.8	— 6.8	2050	19.6	0.63	0.06
20.....	2750	45	7	15.0	21.5	— 6.5	1720	19.3	0.56	0.00
21.....	2750	45	7	15.0	24.4	— 9.4	1520	22.2	0.60	0.03
22.....	2750	45	7	15.0	25.9	—10.9	1730	23.7	0.61	0.00
				Period IV.						
23.....	5490	91	53	15.0	21.7	— 6.7	1320	19.5	0.63	0.03
24.....	5620	94	55	15.0	17.3	— 2.3	1040	15.1	0.63	0.02
25.....	5820	97	59	15.0	15.9	— 0.9	1080	13.7	0.60	0.00
26.....	5530	92	54	15.0	16.5	— 1.5	1600	14.3	0.60	0.00
27.....	5580	93	55	15.0	19.9	— 4.9	1260	17.7	0.64	0.00
28.....	4940	82	47	13.8	17.3	— 3.4	1060	15.1	0.53	0.00
29.....	4940	82	47	13.8	16.7	— 2.8	900	14.5	0.51	0.05
30.....	4940	82	47	13.8	17.9	— 4.0	1100	15.7	0.53	0.02
				Period V.						
31.....	4940	83	48	13.8	12.4	+ 1.4	790	10.3	0.43	0.01
32.....	5180	87	52	13.8	14.2	— 0.4	880	12.1	0.50	....
33.....	5180	87	52	13.8	13.9	— 0.1	840	11.8	0.52	....
1.....	5180	87	52	13.8	11.8	+ 2.0	740	9.7	0.45	....
2.....	5180	87	52	13.8	11.6	+ 2.1	700	9.5	0.47	....
3.....	4200	71	35	13.8	11.6	+ 2.1	860	9.5	0.45	....
				Period VI.						
4.....	2490	42	7	13.8	13.5	+ 0.3	1340	11.4	0.44	....
5.....	2490	42	7	13.8	13.0	+ 0.8	1210	10.9	0.45	....
6.....	2490	42	7	13.8	14.2	— 0.4	1600	12.1	0.46	....
7.....	2240	38	6	12.7	15.0	— 2.3	2000	12.9	0.54	....

* "Excretion"=Total nitrogen of urine + 15 per cent. of food-nitrogen.

TABLE 11.—PATIENT 3, Z—O: AVERAGES FROM PERIODS.
Figures are given for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food. Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion N.	Balance N.	Kreatinin N.	Kreatin N.	Kreatinin Coef.
				Period I.						
4.....	104. -103.2	72	18	48	13.9	14.8	—0.9	0.63	0.05	10.5
				Period II.						
6.....	103.6–102.8	85	32	48	15.0	15.2	—0.2	0.56	0.02	9.2
				Period III.						
4.....	103.8–103.4	45	32	7	15.0	23.5	—8.5	0.60	0.02	10.0
				Period IV.*						
8.....	104.8–101.4	89	31	52	14.5	17.3	—2.8	0.58	0.01	9.6
				Period V.						
6.....	100.8– 99.4	83	29	48	13.8	12.6	+1.2	0.47	....	7.9
				Period VI.						
4.....	Normal	41	28	7	13.5	13.8	(—2.3) —0.3	0.47	....	7.8

* First day of period omitted from average.

TABLE 12.—PATIENT 3, Z—O: DETERMINATIONS MADE IN "COMPOSITE" URINES.
Figures given for 24 hours.

Total N. of Urine.	NH_3 N.	Uric Acid N.	"Rest" N.	Xanthin Bases Mg. Xanthin.	Per Cent. Total N.			Sulphur Gm.				Per Cent. of Total S.			Indican.	Sugar.	Albumin.	Titrated Acidity. N c.c. / 10	Chlorin. Gm.	Total N. / 100×Tot. S.
					Urea.	NH_3.	"Rest."	Total.	Inorganic.	Ethereal.	Neutral.	Inorganic.	Ethereal.	Neutral.						
Period I.																				
12.7	1.91	0.24	1.00	23	71.9	15.0	7.9	1.005	0.726	0.040	0.239	72.2	4.0	23.8	0	Trace	Slight +	520	2.6	7.9
Period II.																				
13.0	1.25	0.24	0.79	38	78.4	9.6	6.1	0.925	0.710	0.037	0.178	76.8	4.0	19.2	0	0	Trace	543	2.2	7.1
Period III.																				
21.0	0.86	0.22	1.09	47	86.9	4.1	5.2	1.408	1.129	0.069	0.210	80.2	4.9	14.9	10	0	Trace	772	2.8	6.7
Period IV.																				
15.6	1.09	0.22	1.14	..	79.6	7.0	7.3	1.155	0.919	0.055	0.181	79.5	4.8	15.7	15	Trace	0	610	2.7	7.4
Period V.																				
10.4	0.77	0.12	0.70	..	79.8	7.5	6.7	0.746	0.580	0.061	0.105	77.7	8.2	14.1	3	0	0	540	2.7	7.2
Period VI.																				
11.5	0.72	0.21	0.62	..	82.2	6.3	5.5	0.810	0.589	0.076	0.145	72.7	9.4	17.9	20	0	0	550	3.6	7.1

determined in the urine of each day as usual, while all of the other determinations were made in "composite" urines representing the whole of the several periods. The latter results are given in Table 12. A summary of results in periods is given in Table 11, and the daily detailed data in Tables 9 and 10.

This is one of the most interesting experiments of the series. During the first period, *at the height of the disease with food equivalent to 72 calories per kg.* and 13.9 gm. nitrogen, the subject *lost only 0.9 gm. nitrogen per day.* The amount of kreatin excreted (0.05 gm. nitrogen) is equivalent to 1.3 gm. muscle-protein-nitrogen. This roughly corresponds to the nitrogen balance and indicates that the nitrogen lost was derived wholly from muscle tissues.

On the other hand, the amount of kreatin excreted as well as the minus balance of nitrogen, was very small. From results of our experiments with other subjects there can be no doubt that with food of lower caloric value this patient would at that time have excreted much kreatin and would have shown a large minus balance of nitrogen during this period. That he did not excrete much kreatin indicates not only a protection afforded to the protein of blood and tissue fluids (circulating protein) from being drawn on as a source of fuel or for other purposes, but a protection of muscle proteins from the mechanism of the "toxic" destruction. Whatever the nature of this protection, it was certainly accomplished by the high caloric value of the food.

In the next period (II) the diet was increased to 85 calories per kg. by the addition of cream; and the subject was practically in nitrogen equilibrium. Only 0.02 gm. of kreatin-nitrogen was excreted, though the temperature was still high, and it seems fair to believe that a pathologic destruction of muscle and other body protein would have taken place but for the large food-supply.

In the third period the diet was kept the same, with the important exception of withdrawing 600 gm. (!) of carbohydrate. The subject received food equivalent to 45 calories per kg., but lost an average of 8.5 gm. nitrogen per day. That the effect of withdrawing carbohydrate is even greater than the above figure indicates is shown by the daily analyses (Table 10). The excretion of nitrogen increased progressively to the last day of the period and might have gone higher. This is probably to be explained by the protection of glycogen stored during the preceding period of high carbohydrate diet. Calculated on the basis of the last two days of the period, the daily loss would be 10.2 gm. of nitrogen.

The kreatin excretion during this period also was small, making it probable that the nitrogen lost was not derived from muscle tissues. Assuming the muscles to be an important seat of the "toxic" destruction, it is surprisng that in this period, when much body nitrogen was being lost, the muscle protein was not being in part drawn on. It may be that the muscles are protected until the circulating protein has sustained a certain loss, or in this instance the muscles may have been protected during this period of four days by a reserve supply of glycogen accumulated during the previous periods. This explanation is not wholly satisfactory; but the fact remains that those of our subjects who were not given diets of high caloric value excreted, as a rule, much kreatin at the time when they were losing much body protein, while those who received food of high fuel value excreted much less kreatin and, even on withdrawing fat or carbohydrate, these latter patients showed, as a rule, no very considerable amounts of kreatin in the urine. And if our premise is correct, that the appearance of endogenous kreatin in the urine indicates the destruction of muscle protein, the conclusion is warranted that by the diets of large caloric value we in some way protect the muscle tissues from this pathologic katabolism.

In the fourth period much carbohydrate was again added, the food representing 89 calories per kg., 52 of which were in the form of carbohydrate. Excluding the first day of the period, the average balance was minus 2.8 gm. of nitrogen. Why the loss was greater here than in Period II is not clear, but it was much less than in Period III.

During half of Period V the subject had a normal temperature. With food equivalent to 83 calories per kg. there was an average daily gain of 1.2 gm. nitrogen. In Period VI most of the carbohydrate was again withdrawn and the nitrogen excretion rose, giving on the last day a minus balance of 2.3 gm. nitrogen. The temperature was normal and the food contained 13.5 gm. nitrogen and 41 calories per kg. The average balance (—0.3 gm.) does not fairly represent the period because of the effect, during the first days, of the carbohydrate stored from the preceding period.

Patient 4—W—d, male 23 years of age ,hotel clerk, well-nourished, taken ill one week before admission. Illness severe. Fever lasted twenty-six days, with mild relapse of seven days' duration. Blood-culture negative. The serum did not react to

TABLE 13.—PATIENT 4, W—D: TEMPERATURE AND FOOD.

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food. Milk.	Lactose.	Toast.	Butter.	Protein.	Fat.	C. H.
				Period I.						
10	....	104.4	102.6	2160	....	....	....	71.3	108	108
11	....	104.4	103.2	2160	....	....	....	71.3	108	108
12	....	103.8	102.6	2400	....	....	....	79.2	120	120
13	63.?	103.6	102.0	2340	....	....	....	77.2	116	116
14	....	103.6	102.0	2400	....	....	....	79.2	120	120
15	....	103.6	102.4	2400	....	....	....	79.2	120	120
16	....	103.4	101.8	2400	....	....	....	79.2	120	120
17	....	103.2	101.8	2400	....	....	....	79.2	120	120
18	....	102.6	101.6	2400	....	....	....	79.2	120	120
Average								78.9	119	119
				Period II.						
19	....	102.8	101.0	2400	450	....	....	79.2	120	570
20	....	102.4	101.0	2400	405	....	....	79.2	120	525
21	....	101.0	99.6	2400	450	....	....	79.2	120	570
22	....	102.2	99.8	2400	585	....	....	79.2	120	705
23	....	100.6	99.6	2400	600	....	....	79.2	120	720
24	61.0	100.6	99.0	2310	560	....	....	76.2	116	676
Average								78.7	119	628
Normal Temperature.				Period III.						
1	....	99.8	98.8	2400	....	....	....	79.2	120	120
2	....	99.4	98.8	2400	....	....	....	79.2	120	120
3	60.2	99.2	98.4	2400	....	....	....	79.2	120	120
4	59.8	98.8	98.0	2400	....	....	....	79.2	120	120
5	....	100.0	98.2	2400	....	....	....	79.2	120	120
Relapse.										
1	....	100.8	99.2	2400	....	90	4	89.0	123	174
Average								79.2	120	120
				Period IV.						
2	....	102.4	99.4	2400	505	90	8	89.0	127	679
3	....	102.8	100.6	2400	600	90	48	89.0	161	774
4	61.6	102.8	100.8	2400	600	60	32	85.8	147	756
5	....	101.2	100.0	2400	600	90	24	89.0	140	756
6	61.4	100.2	99.0	2400	600	90	24	89.0	140	756
Convalescence.										
....	....	99.8	98.6	2400	600	90	24	89.0	140	756
2	62.3	99.6	98.0	2400	600	90	24	89.0	140	756
3	....	99.6	98.0	2400	600	90	16	89.0	134	756
Average								88.5	143	754
				Period V.						
4	62.7	99.2	98.0	2400	....	90	24	89.0	140	174
5	....	99.4	98.0	2400	....	90	24	89.0	140	174
6	....	99.2	98.0	2160	....	90	16	81.2	121	162
7	....	99.6	97.6	2400	....	120	24	93.4	140	192
8	63.0	99.4	97.8	2400	....	120	48	93.4	161	192
9	....	99.4	97.6	2400	....	120	48	93.4	161	192
Average								90.1	145	182

TABLE 14.—PATIENT 4, W—D: DAILY NITROGEN BALANCE AND URINE.

Day of Disease.	Calories. Total.	Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance. Intake.	Excretion.	Balance.	Urine. Volume c.c.	Nitrogen as Total.	Kreatinin.	Kreatin.
					Period I.*					
10	1740	28	07.0	11.4	....	.....	1010	12.4	0.78	....
11	1740	28	07.0	11.4	18.0	— 6.6	1320	16.7	0.67	....
12	1930	31	07.8	12.7	25.2	—12.5	2300	23.9	0.82	....
13	1870	30	07.5	12.3	25.0	—12.7	1570	23.7	0.68	....
14	1930	31	07.8	12.7	24.7	—12.0	2330	23.4	0.70	....
15	1930	31	07.8	12.7	23.9	—11.2	2300	22.6	0.69	....
16	1930	31	07.8	12.7	22.9	—10.2	2550	21.6	0.65	....
17	1930	31	07.8	12.7	23.3	—10.6	2100	22.0	0.62	....
18	1930	31	07.8	12.7	22.6	— 9.9	1660	21.3	0.66	....

Day of Disease.	Calories. Total.	Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance. Intake.	Excretion.	Balance.	Urine. Volume c.c.	Nitrogen as Total.	Kreatinin.	Kreatin.
					Period II.					
19.....	3770	60	38.0	12.7	....	.....	2060	19.7	0.60	0.05
20.....	3600	57	35.0	12.7	....	.....	2210	16.4	0.59	0.02
21.....	3770	60	38.0	12.7	....	.....	1660	14.9	0.63	....
22.....	4320	70	47.0	12.7	13.6	— 0.9	1320	11.7	0.45	....
23.....	4390	72	48.0	12.7	13.3	— 0.6	2000	11.4	0.48	....
24.....	4160	68	45.0	12.2	14.2	— 2.0	1790	12.4	0.49	....
Normal Temperature.					Period III.					
1.....	1930	32	08.0	12.7	....	.....	2300	13.9	0.46	....
2.....	1930	32	08.0	12.7	17.0	— 4.3	2050	15.1	0.45	....
3.....	1930	32	08.0	12.7	16.7	— 4.0	2080	14.8	0.44	....
4.....	1930	32	08.0	12.7	16.3	— 3.6	2010	14.4	0.43	....
5.....	1930	32	08.0	12.7	15.3	— 2.6	2000	13.4	0.45	....
Relapse.										
1.....	2220	37	12.0	14.2	15.9	— 0.9	1720	13.0	0.54	0.00
					Period IV.					
2.....	4330	72	46.0	14.2	....	.....	1820	11.2	0.61	0.00
3.....	5040	83	52.0	14.2	11.0	+ 3.2	2000	8.9	0.61	0.00
4.....	4830	79	50.0	13.7	10.3	+ 3.4	1930	8.1	0.57	0.00
5.....	4760	78	50.0	14.2	10.8	+ 3.4	1720	8.7	0.56	0.00
6.....	4760	78	50.0	14.2	10.5	+ 3.7	1730	8.4	0.47	0.03
Convalescence.										
1.....	4760	77	50.0	14.2	11.1	+ 3.1	1320	9.0	0.47	0.02
2.....	4760	77	50.0	14.2	10.3	+ 3.9	1730	8.2	0.44	....
3.....	4710	76	50.0	14.2	9.8	+ 4.4	1420	7.7	0.45	0.00
					Period V.					
4.....	2380	38	11.0	14.2	....	.....	1620	9.2	0.43	0.02
5.....	2380	38	11.0	14.2	11.9	+ 2.3	1770	9.8	0.41	0.00
6.....	2130	34	11.0	13.0	12.0	+ 1.0	1600	9.9	0.45	0.01
7.....	2470	39	13.0	14.9	12.8	+ 2.1	2300	10.6	0.45	0.02
8.....	2670	43	13.0	14.9	12.5	+ 2.4	2000	10.3	0.46	0.00
9.....	2670	43	13.0	14.9	13.5	+ 1.4	2180	11.3	0.43	0.05

* Feces in Period I contained 1.26 gm. nitrogen per day.
Excretion in Period I = total nitrogen of urine + 1.26 gm.
Excretion in other periods = total nitrogen of urine + 15 per cent. of food nitrogen.

TABLE 15.—PATIENT 4. W—4: AVERAGES FROM PERIODS.

No. of Days.	Range of Maximum Temp. F. During Period.	Food. Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion N.	Balance N.	Kreatinin N.
				Period I.				
9.....	104.4–102.6	31	18	8	12.6	23.9*	—11.3	0.69
				Period II.				
6.....	102.8–100.6	65	18	42	12.6	13.7†	— 1.1	0.54
				Period III.				
6.....	99.8–100.8	32	18	8	12.7	16.3‡	— 3.6	0.44
				Period IV.				
8.....	102.4– 99.6	77	21	50	14.2	10.5§	+ 3.7	0.51
				Period V.				
6.....	Normal	40	22	12	14.4	12.6	+ 1.8	0.44

* First two days of period excluded from average.
† First three days of period excluded from average.
‡ First and last days of period excluded from average.
§ First day of period excluded from average.

the typhoid bacillus but was not tried against the intermediates. The whole clinical picture, however, was that of typhoid fever.

The experiment with this patient is to some extent the opposite of the last described (Z—o), and again shows very strikingly the great protection from the loss of body protein afforded by food rich in carbohydrate.

The daily detailed results are given in Tables 13 and 14: Table 15 contains the averages of periods for the nitrogen balance, etc.: and Table 16 the results of sulphur and nitrogen partitions in composite urines representing the several periods.

TABLE 16.—PATIENT 4, W—D: DETERMINATIONS MADE IN "COMPOSITE" URINES—AVERAGES FOR 24 HOURS.

"Rest" N.	Total N.	NH_3 N.	Uric Acid N.	Xanthin Bases Mg. Xanthin.	Per Cent. Total N.			Sulphur Gm.				Per Cent. of Total S.			Chlorin. Gm.	Titrated Acidity. N c.c. / 10	Indican.	Sugar.	Albumin.	100 × Tot. S. / Total N.
					Urea.	NH_3.	"Rest."	Total.	Inorganic.	Ethereal.	Neutral.	Inorganic.	Ethereal.	Neutral.						
									Period I.											
21.0	0.93	0.29	1.10	91	85.6	4.4	5.2	1.570	1.090	0.090	0.390	69.5	5.7	24.8	1.9	420	10	0	Trace	7.5
									Period II.											
14.4	0.65	0.23	1.13	37	82.7	4.4	7.5	1.000	0.731	0.034	0.235	73.1	3.4	23.5	1.5	250	20	0	0	7.0
									Period III.											
14.2	0.36	0.19	0.56	53	89.0	2.5	4.0	0.901	0.704	0.032	0.165	78.2	3.5	18.3	1.8	210	8	0	0	6.35
									Period IV.											
8.7	0.40	0.17	0.77	30	78.5	4.7	8.8	0.638	0.461	0.048	0.129	72.3	7.5	20.2	2.3	240	10	0	0	7.35
									Period V.											
10.3	0.32	0.18	0.60	87	85.3	3.1	5.8	0.672	0.521	0.005?	0.146	77.4	0.8?	21.8	3.3	184	20	0	0	6.5

During the first nine days of the experiment, which began on the tenth day of the disease and continued for thirty-five days, the patient received a strict milk diet, so frequently used in typhoid fever. The food was equivalent to 31 calories per kg. and contained 12.6 gm. of nitrogen. Excluding the first two days of this period, which clearly show the effect of food of high fuel value given during several days before the beginning of the experiment, the average loss per day was 11.3 gm. of nitrogen. Kreatin unfortunately was not determined during this period. During the following six days the food remained the same, except for the addition of much carbohydate in the form of lactose, the average fuel value of the diet then being 65 calories per kg. There resulted a rapid decline of the nitrogen excretion so that, on the last three of the six days of the period, the subject lost only 1.1 gm. nitrogen each day. This result is perhaps due in part to the simultaneous fall in temperature; but that the added carbohydrate was very largely responsible is shown by the next period (III), when the patient had a normal temperature except on one day. The lactose was withdrawn and there was at once an increase in the nitrogen excretion, giving an average minus balance of 3.6 gm. (32).

Except for the one day on which the temperature rose to 100.8 F. and which is excluded from the average, this was clinically a period (III) of convalescence; and yet with food equivalent to 32 calories per kg. and to 12.7 gm. of nitrogen the subject lost 3.6 gm. of body nitrogen per day. The conclusion seems warranted that the food was not of sufficient fuel value to prevent or compensate for the excessive protein destruction which was still taking place. It is obvious that the excessive protein katabolism of this period was not due to pyrexia since the departure was normal.

The following period (IV) includes five days of a relapse and three days of normal temperature. Food of high fuel value, 77 calories per kg., was given throughout and the subject gained nitrogen on each day of the period, the average balance being plus 3.7 gm. Practically no kreatin was excreted. The interpretation seems wholly justified that the large food-supply, consisting chiefly of carbohydrates, completely prevented in this instance the excess of protein katabolism which undoubtedly would otherwise have taken place.

During Period III the temperature was normal, but the subject lost 3.6 gm. nitrogen each day on a diet containing 32 total calories and 8 carbohydrate calories per kg.; during period IV, in spite of relapse during five of the eight days, he gained 3.7 gm. nitrogen each day on a diet containing 77 total calories and 50 carbohydrate calories per kg. As compared with Period III there was a sparing during Period IV of at least 7.3 gm. (3.7—[—3.6]=7.3) of nitrogen per day, which gain is presumably wholly referable to the difference in diet.

Food.	Period III gm.	Period IV gm.
Total cal. per kg	32.0	77.0
Total cal. per kg	32.0	77.0
Carbohydrate cal. per kg	8.0	50.0
Fat—cal. per kg	18.0	21.0

The only marked difference in the diets is in the carbohydrate calories. It appears fair to interpret these figures as showing that the addition of 42 carbohydrate calories per kg. has in this patient spared 7.3 gm. nitrogen or 45.5 gm. of body protein.

In the last period, with normal temperature, the subject showed an average plus balance of 1.8 gm. of nitrogen on a diet equivalent to 40 calories per kg. The increased katabolism had probably ceased and the food was, under the conditions, more than sufficient to maintain equilibrium. The situation here is in sharp contrast with that in Period III when, with normal temperature and food equivalent to 32 calories per kg., a minus balance of 3.6 gm. was observed; in the latter period the pathologic increase in katabolism was doubtless still taking place.

The comparison of the results in these two periods of normal temperature again illustrates the importance of the intensity of the katabolic process in determining the degree of sparing of body protein accomplished by any given food. This factor explains the difficulty in comparing, quantitatively, a result from one subject with that of another, or even the results from two different periods on the same subject.

Patient 5—B—t, male, 23 years of age, driver, well-nourished, admitted to hospital on seventh day of disease. Positive blood-culture. Illness moderately severe.

TABLE 17.—PATIENT 5, B—T: DAILY TEMPERATURE AND FOOD.

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Milk c.c.	Cream c.c.	Eggs.	Lactose Gm.	Toast Gm.	Butter Gm.	Somatose Gm.	Protein Gm.	Fat Gm.	C. H. Gm.
Period I.													
9	....	103.2	101.0	2070	90	1	110	....	24	....	77.4	138	216
10	....	103.8	102.2	1290	480	2	140	60	82	....	73.0	289	255
11	....	103.6	102.4	1320	480	2	140	60	96	....	74.0	292	240
12	75.?	103.2	100.6	1260	420	1	170	90	69	....	67.0	253	300
13	....	?	....	1290	570	1	170	90	69	....	71.0	299	305
14	....	101.8	100.0	1290	600	1	170	90	69	....	71.0	308	306
15	....	101.8	99.0	1440	540	3	170	90	69	....	90.0	309	312
16	....	101.6	99.2	1320	810	3	160	90	100	....	91.0	410	294
Average											76.8	287	279
Period II.													
17	....	100.6	98.4	2000	....	3	540	90	100	....	97.5	201	694
18	74.?	100.4	98.8	2000	....	3	500	90	84	....	97.5	187	654
19	....	100.2	98.8	2100	....	3	560	120	75	....	104.0	185	737
20	....	100.0	99.8	2100	....	3	560	120	79	....	104.0	188	737
21	....	100.0	98.4	2040	....	3	560	120	79	....	102.0	185	734
22	73.0	100.4	98.6	2000	....	3	495	120	111	....	101.0	210	667
Average											101.0	193	704
Period III.													
23	....	100.2	98.6	2000	....	3	....	120	64	....	101.0	170	172
24	....	99.4	98.4	2000	....	3	....	120	80	....	101.0	184	172
25	72.9	99.8	98.0	2000	....	3	....	120	80	....	101.0	184	172
Relapse.													
1	72.7	100.4	98.4	2000	....	3	....	120	80	....	101.0	184	172
2	....	101.6	99.2	2000	....	3	....	120	80	....	101.0	184	172
Average											101.0	184	172
Period IV.													
3	....	?	....	2000	....	3	....	120	80	60	147.0	184	172
4	73.0	102.2	100.8	2000	....	3	....	120	80	60	147.0	184	172
5	....	101.8	99.8	2000	....	3	....	120	80	50	131.0	184	172
Average											142.0	184	172
Period V.													
6	73.2	?	99.6	2000	....	3	600	120	80	....	101.0	184	772
7	....	100.8	99.4	2000	60	3	600	120	80	....	102.0	202	775
8	....	100.4	99.0	2000	....	3	600	120	80	....	101.0	184	772
Convalescence.													
1	73.1	99.8	98.0	1800	....	4	540	120	80	....	101.0	179	700
2	....	99.6	98.4	2000	....	4	600	120	80	....	108.0	189	772
3	73.9	99.6	98.0	2000	....	4	600	120	80	....	108.0	189	772
4	....	98.8	98.0	2000	....	4	600	120	80	....	108.0	189	772
5	....	99.8	98.0	2000	....	4	600	120	80	....	108.0	189	772
6	....	99.6	98.2	2000	....	4	600	120	80	....	108.0	189	772
7	74.8	99.8	98.0	2000	....	4	600	120	80	....	108.0	189	772
8	....	99.4	98.0	2000	....	4	600	120	80	....	108.0	189	772
9	....	99.6	98.0	2000	....	4	600	120	80	....	108.0	189	772
Average											107.0	188	765

TABLE 18.—PATIENT 5, B—T: DAILY NITROGEN BALANCE AND URINE.

Day of Disease.	Calories. Total.	Calories. Per Kg.	C. H. Cal. Per Kg.	Nitrogen Balance. Intake.	Excretion.*	Balance.	Urine. Volume c.c.	Nitrogen as Total.	Kreatinin.	Kreatin.
				Period I.						
9.....	2480	33	12.0	12.4	18.4	—6.0	655	16.5	0.80	....
10.....	4040	54	14.0	11.7	15.6	—3.9	630	13.9	0.68	....
11.....	4030	54	13.0	11.8	17.4	—5.6	920	15.6	0.77	....
12.....	3860	51	16.0	10.7	19.2	—8.5	1420	17.6	0.88	....
13.....	4320	58	17.0	11.3	17.0	—5.7	1080	15.3	0.81	....
14.....	4400	59	17.0	11.3	18.0	—6.7	880	16.3	0.82	....
15.....	4530	61	17.0	14.4	18.0	—3.6	950	15.8	0.74	....
16.....	5400	72	16.0	14.5	19.3	—4.8	1150	17.1	0.67	....
				Period II.						
17.....	5120	69	38.0	15.6	19.1	—3.5	1220	16.8	0.67	0.08
18.....	4820	65	36.0	15.6	18.3	—2.7	1310	16.0	0.63	0.08
19.....	5170	70	41.0	16.6	20.6	—4.0	1620	18.1	0.65	....
20.....	5200	70	41.0	16.6	20.4	—3.8	1520	17.9	0.61	....
21.....	5150	70	41.0	16.3	20.3	—4.0	1680	17.9	0.61	....
22.....	5100	70	38.0	16.1	19.7	—3.6	1580	17.3	0.62	....
				Period III.						
23.....	2740	38	9.6	16.1	....	.....	1570	17.5	0.59	....
24.....	2870	39	9.6	16.1	23.6	—7.5	1850	21.2	0.63	....
25.....	2870	39	9.6	16.1	23.8	—7.7	1700	21.4	0.63	....
Relapse.										
1.....	2870	39	9.6	16.1	24.6	—8.5	1900	22.2	0.65	....
2.....	2870	39	9.6	16.1	23.7	—7.6	1540	21.3	0.65	....
				Period IV.						
3.....	3020	41	9.6	23.5	27.2	—3.7	1850	23.7	0.89	....
4.....	3020	41	9.6	23.5	27.5	—4.0	2920	24.0	0.84	....
5.....	2950	40	9.6	21.0	28.9	—7.9	1820	25.4	0.80	....
				Period V.						
6.....	5290	72	43.0	16.1	....	.....	1500	19.5	0.72	....
7.....	5470	75	43.0	16.3	....	.....	1780	20.5	0.72	0.04
8.....	5290	72	43.0	16.1	17.4	—1.3	1550	15.0	0.61	0.07
Convalescence.										
1.....	4950	68	39.0	16.1	16.6	—0.5	1500	14.2	0.62	0.01
2.....	5370	73	43.0	17.3	17.7	—0.4	1320	15.1	0.59	0.05
3.....	5370	73	43.0	17.3	17.8	—0.5	1140	15.2	0.60	0.00
4.....	5370	73	43.0	17.3	17.6	—0.3	1460	15.0	0.62	0.00
5.....	5370	72	43.0	17.3	17.5	—0.2	1530	14.9	0.63	0.00
6.....	5370	72	43.0	17.3	17.4	—0.1	1430	14.8	0.67	....
7.....	5370	72	43.0	17.3	17.2	+0.1	1230	14.6	0.62	0.02
8.....	5370	72	43.0	17.3	17.4	—0.1	1540	14.8	0.57	0.07
9.....	5370	72	43.0	17.3	17.1	+0.2	1520	14.5	0.62	0.00

* "Excretion" = total nitrogen of urine + 15 per cent. of food-nitrogen.

TABLE 19.—PATIENT 5, B—T: AVERAGES FROM PERIODS.

No. of Days.	Range of Maximum Temp. F. During Period.	Food. Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen Gm.	Excretion N.	Balance N.	Kreatinin N.	Kreatin N.
				Period I.					
8.....	103.8–101.6	56	36	16	12.3	17.8	—5.5	0.77	....
				Period II.					
6.....	100.8–100.0	69	24	39	16.2	19.7	—3.5	0.63	0.08
				Period III.					
5.....	101.6– 99.4	39	23	9	16.1	23.9*	—7.8	0.64	....
				Period IV.					
3.....	102.2–101.8	40	23	9	22.7	28.9†	—6.2	0.84	....
				Period V.					
12.....	100.8– 99.4	72	24	43	17.1	17.3‡	—0.2	0.63	0.02

* First day of period excluded from average.
† Excretion of last day taken as representing period.
‡ First two days of period excluded from average.

TABLE 20.—PATIENT 5, B—T: DETERMINATIONS MADE IN "COMPOSITE" URINES.
Figures given are for 24 hours.

Total N.	NH_3 N.	Uric Acid N.	"Rest" N.	Xanthin Bases Mg. Xanthin.	Per Cent. Total N.			Sulphur Gm.				Per Cent. of Total S			Chlorin. Gm.	Titrated Acidity. N c.c. 1/10	Indican.	Sugar.	Albumin.	100×Total S. / Total N.
					Urea.	NH_3.	"Rest."	Total.	Inorganic.	Ethereal.	Neutral.	Inorganic.	Ethereal.	Neutral.						
								Period I.												
16.0	1.49	0.21	0.52	27	80.7	9.3	3.2	1.140	0.845	0.015	0.280	74.1	1.3	24.6	2.3	530	30	0	Trace	7.1
								Period II.												
17.0	0.90	0.21	0.70	44	85.1	5.3	4.1	1.192	0.941	0.047	0.204	79.0	3.9	17.1	4.1	660	80	0	0	7.0
								Period III.												
20.5	1.35	0.23	1.60	73	81.3	6.6	7.8	1.353	.....	.....	0.190	....	...	14.0	...	...	..	0	0	6.6
								Period IV.												
24.3	0.77	0.27	2.30	81	82.8	3.2	9.5	1.660	1.405	0.040	0.215	84.7	2.4	12.9	4.3	615	6	0	0	6.8
								Period V.												
15.5	0.89	0.22	0.60	73	84.6	5.7	3.9	1.150	0.928	0.032	0.190	80.7	2.8	16.5	4.5	640	20	0	0	7.4

This experiment was intended primarily to determine the relative value of fat versus carbohydrate in protecting the body protein in fever, but it was not carried out as planned and the conclusion on this point is not clear. The experiment does again show the marked effect of carbohydrate, and is of interest also for other reasons.

The experiment began on the ninth day of the disease and continued for thirty-four days, including fifteen days of the original fever and a relapse of eight days. The averages representing the five periods into which the experiment is divided are given in Table 19. Other data are given in Tables 17, 18 and 20.

During the first period of eight days at the height of the disease, the fuel value of the food averaged 56 calories per kg., of which 36 were in fat and 16 in carbohydrates. The subject lost 5.5 gm. nitrogen per day. In the next period (II) the fat was in part withdrawn and more carbohydrate added ,so that the average daily food equaled 69 calories per kg., of which 39 were in carbohydrate and 24 in fat. The loss of nitrogen was decreased by 2 gm. The situation is, however, complicated by the lower temperature and the higher total caloric and protein value of the food in the second period; and no conclusion seems to be justified regarding the relative value of fat versus carbohydrate in retarding the loss of nitrogen. There was, however, a marked sparing effect in both of these periods, as shown by Period III, when the temperature was lower than before. The food contained practically the same amount of nitrogen (16.1 gm.) as in Period II, but was equivalent to only 39 calories per kg.; excluding the first day, the average loss was 7.8 gm. nitrogen. On two days of this period the temperature remained below 100 F., while on two other days the highest temperature was only 100.2 and 100.4 F., respectively. On the last day of the period a relapse set in and the temperature reached 101.6. Except on this last day, the patient might be considered clinically almost in the condition of convalescence, but with food, which under normal circumstances would have maintained equilibrium, he lost more than twice as much body nitrogen as in the previous period (II). Even assuming the intensity of the katabolic processes to have been no greater in Period II than in III—and it probably was greater—the additional carbohydrate of Period II (equivalent to about 30 cal. per kg.) appears to have accomplished a sparing of 4.3 gm. nitrogen per day.

During the next three days (Period IV), in the midst of a relapse, the protein intake was increased by the addition of "somatose" to between 21 and 23.5 gm. nitrogen, the total fuel value of the diet remaining at about 40 calories per kg. On account of the lag in excretion, the first two days of the period are excluded and the last day is taken to represent the period. On this day the loss of nitrogen was 7.9 gm., indicating no advantage from the increase of protein intake, though this conclusion is rendered somewhat uncertain by the relapse and the consequent probable further increase in the katabolism of body protein.

During at least the last nine of the twelve days of Period V the subject was in what would ordinarily be called a convalescent condition. His temperature was normal, and clinically his disease was at an end. But, in spite of diet of high caloric value (72 calories per kg.) and containing 17.1 gm. of nitrogen, there was a small loss of body nitrogen throughout the period. A loss of 0.2 gm. of nitrogen per day, of course, is not great and, if less than the estimated 15 per cent. of the food nitrogen was excreted in the feces, there may even have been an actual slight gain of nitrogen. But this difference is of little consequence: the significant thing is that the subject was not gaining three or four grams of nitrogen each day which, according to other experiments, he should have done on such a diet unless a pathologic increase in metabolism was persisting after the fall of temperature. We are inclined to interpret the result in this way: that in this period, as in Period III, the pathologic increase in katabolism continued after the temperature became normal and after the disease was apparently at an end, and that a considerable loss of body nitrogen was prevented by the large food-supply.

Patient 6—L—d. male, 32 years of age, waiter, fairly well nourished. Moderately severe illness, with a relapse of thirteen days. Positive serum reaction with typhoid bacilli.

The experiment began on the seventeenth day of the disease, almost at the end of fever, and continued for forty-three days, including a relapse of thirteen days' duration. The detailed results are given in Tables 21, 22 and 23, and the averages of periods in Table 24.

During the first period of four days, representing the end of the fever, the patient received food equivalent to 24 calories per kg. and containing 10 gm. of nitrogen. A daily minus balance of 8.3 gm. of nitrogen was found, and 0.11 gm. of kreatin-nitrogen was excreted. Both of these results are of very considerable interest, showing, as they

do, that, with a somewhat inadequate food-supply, the protein katabolism was still very markedly increased, when the disease, as indicated by the temperature and clinical condition of the subject, had practically run its course. Attention is particularly called to the considerable excretion of kreatin at this time.

In the second period of six days, during which the temperature was normal, the energy value of the food was doubled (51 cal. per kg.), which was immediately followed by a sharp decline in the excretion of nitrogen and of kreatin as well.

Excluding the first day of the period, in which the effect of the high caloric diet is not seen, the averages for the period are: a minus balance of 1.1 gm. nitrogen (as compared with 8.3 gm. of the preceding period), and 0.03 gm. kreatin-nitrogen.

Four of the six days of Period III were the beginning of a relapse. The patient received food equivalent to 58 cal. per kg. and containing 12.9 gm. of nitrogen. Excluding the first day of the period, the urine of which was lost, there was an average plus balance of 0.6 gm. nitrogen and 0.06 gm. kreatin-nitrogen; the kreatin indicating a somewhat greater absorption of muscle protein, which was more than compensated for by the retention of other protein. The next five days, Period IV, representing the height of the relapse, the patient received food equal to 55 calories per kg. and 10.8 gm. nitrogen, nearly as much as in the preceding period, but this was not sufficient to counterbalance or prevent a marked increase in the protein katabolism, and the subject lost an average of 3.8 gm. nitrogen each day. This loss, however,

TABLE 21.—PATIENT 6, L—D: DAILY TEMPERATURE AND FOOD.

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food. Milk.	Cream.	Eggs.	Lactose.	Toast.	Protein.	Fat.	C. H.
				Period I.							
17	64.5	102.2	99.0	1770	....	..	....	..	58.5	88.5	88.5
18	....	101.4	99.4	1920	....	..	....	..	63.4	96.0	96.0
19	64.0	100.0	99.8	1920	....	..	....	..	63.4	96.0	96.0
20	....	99.4	98.2	1920	....	..	....	..	63.4	96.0	96.0
	Average								62.2	94.0	94.0
				Period II.							
Normal Temperature.											
1	....	98.8	97.6	1660	90	..	90	..	57.3	111.0	176.0
2	63.0	99.4	97.8	1680	180	..	210	..	59.0	138.0	300.0
3	....	99.0	98.0	2000	230	..	285	..	70.6	169.0	392.0
4	....	98.6	98.2	1680	120	..	300	..	58.0	120.0	387.0
5	....	98.6	98.2	2000	285	..	285	..	71.7	185.0	393.0
6	62.3	99.2	98.2	1700	180	1	300	..	66.8	144.0	390.0
	Average (excluding first day)								65.2	151.0	372.0
				Period III.							
7	....	99.6	97.8	1460	180	3	270	..	73.4	143.0	348.0
8	....	99.6	98.4	1210	165	3	225	..	65.0	126.0	290.0
Relapse.											
1	63.5	101.6	98.2	1910	285	3½	360	60	100.5	200.0	499.0
2	....	103.0	99.6	1680	225	3	315	60	88.0	167.0	442.0
3	64.0	103.2	100.6	1890	315	..	360	..	68.6	188.0	464.0
4	63.2	102.8	101.2	1950	180	2	360	..	82.3	162.0	464.0
	Average (excluding first day)								80.9	169.0	432.0
				Period IV.							
5	....	103.4	100.4	1910	270	1	345	..	75.6	152.0	448.0
6	63.7	103.4	101.2	1760	295	..	295	..	64.0	176.0	393.0
7	....	104.2	101.6	1710	405	2	210	..	78.6	220.0	308.0
8	64.0	103.4	101.4	1160	600	2	105	..	64.7	248.0	180.0
9	....	102.0	100.4	830	630	2	225	..	54.4	240.0	285.0
	Average								67.5	207.0	323.0
				Period V.							
10	64.0	101.6	100.0	960	600	6	365	..	87.0	260.0	430.0
11	....	101.5	99.6	1080	360	6	570	..	86.0	194.0	635.0
12	....	100.0	99.4	1080	360	6	690	..	86.0	194.0	755.0
13	....	99.8	98.8	1080	360	5.5	690	..	83.0	191.0	755.0
Convalescence.											
..	....	99.4	99.0	1080	360	6	690	..	86.0	194.0	755.0
2	....	99.4	98.6	1080	360	6	540	..	86.0	194.0	605.0
3	....	99.2	98.6	1080	360	6	690	..	86.0	194.0	755.0
4	....	99.4	98.8	1120	300	6	690	..	86.0	178.0	755.0
	Average (excluding last day. Urine lost)								86.0	203.0	670.0

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Food. Milk.	Cream.	Eggs. Food.	Lactose.	Toast.	Protein.	Fat.	C. H.
				Period VI.							
5	64.5?	99.6	98.6	1080	360	6	....	..	86.0	194.0	65.0
6	....	99.8	98.4	1080	360	6	....	..	86.0	194.0	65.0
7	....	99.6	98.4	1190	250	6	....	..	87.0	166.0	67.0
8	65.1	99.8	98.0	1080	360	6	....	..	86.0	194.0	65.0
9	....	99.6	98.2	1080	360	6	....	..	86.0	194.0	65.0
	Average								86.0	102.0	65.0
				Period VII.							
10	....	99.6	98.6	1080	360	6	540	..	86.0	194.0	605.0
11	66.7	99.6	98.2	1080	360	6	690	..	86.0	194.0	755.0
12	....	99.4	98.4	1080	360	6	660	..	86.0	194.0	725.0
13	68.1	99.6	98.6	930	350	6	690	..	81.0	184.0	746.0
14	....	100.0	97.8	1080	360	6	440	..	86.0	194.0	505.0
15	....	99.6	97.6	1080	360	6	360	..	86.0	194.0	425.0
16	....	99.6	98.2	1080	360	6	360	..	86.0	194.0	425.0
17	....	100.0	98.4	1080	360	6	360	..	86.0	194.0	425.0
18	....	100.4	98.2	900	360	6	360	..	80.0	185.0	416.0
19	....	99.2	98.4	1080	360	6	360	..	86.0	194.0	425.0
	Average								84.9	192.0	545.0

TABLE 22.—PATIENT 6, L—D: DAILY ANALYSES OF URINE.

Day of Disease.	Volume c.c.	Urine Nitrogen as Total.	NH_3.	Kreatinin.	Kreatin.	Uric Acid.	"Rest."	Per Cent. Total N. Urea.	NH_3.	"Rest."
					Period I.					
17.....	1590	16.5	0.95	0.47	0.07	0.30	0.80	84.4	5.7	4.8
18.....	Urine lost.									
19.....	1520	18.1	1.08	0.47	0.10	0.27	0.60	86.2	6.0	3.3
20.....	1930	15.8	0.97	0.36	0.16	0.24	0.60	85.3	6.2	3.8
					Period II.					
Normal Temperature.										
1.....	1900	15.5	0.91	0.40	0.14	0.22	0.63	85.2	5.9	4.1
2.....	1200	11.6	0.76	0.35	0.07	0.18	0.43	84.7	6.6	3.7
3.....	1380	10.9	0.73	0.34	0.08	0.17	0.68	81.7	6.7	6.3
4.....	1590	10.2	0.60	0.40	0.00	0.13	0.66	82.5	5.9	6.5
5.....	1440	8.1	0.56	0.39	0.00	0.12	0.52	80.7	6.8	6.4
6.....	1480	9.1	0.59	0.42	0.01	0.11	0.40	82.9	6.5	4.4
					Period III.					
7.....	Urine lost.									
8.....	1040	9.0	0.62	0.44	0.00	0.13	0.56	80.7	6.8	6.2
Relapse.										
1.....	840	11.4	0.72	0.50	0.00	0.13	0.60	82.7	6.3	5.3
2.....	2040	10.9	0.82	0.52	0.08	0.12	0.55	80.7	7.5	5.0
3.....	2340	10.4	0.86	0.49	0.13	0.14	0.55	79.2	8.3	5.3
4.....	1540	10.5	0.84	0.52	0.02	0.16	0.64	79.2	8.0	6.1
					Period IV.					
5.....	1940	12.9	0.96	0.53	0.00	0.19	0.75	71.1	7.4	5.8
6.....	1450	12.5	0.92	0.51	0.03	0.19	0.87	80.1	7.3	7.0
7.....	1940	14.6	1.23	0.56	0.03	0.20	0.94	79.8	8.4	6.5
8.....	2290	13.7	....	0.48	0.02	....	....	....	....	....
9.....	1920	11.5	....	0.45	0.01	....	....	....	....	....
					Period V.					
10.....	1640	10.1	....	0.43	0.00	....	....	....	....	....
11.....	2450	8.2	....	0.43	0.00	....	....	....	....	....
12.....	1600	7.7	....	0.39	0.00	....	....	....	....	....
13.....	1900	7.7	....	0.40	0.00	....	....	....	....	....
1.....	1600	7.6	....	0.40	0.00	....	....	....	....	....
3.....	1740	7.4	....	0.40	0.04	....	....	....	....	....
3.....	1580	6.8	....	0.36	0.01	....	....	....	....	....
4.....	Urine lost.									
					Period VI.					
5.....	2330	9.6	....	0.41	....	....	....	....	....	....
6.....	1950	10.9	....	0.36	....	....	....	....	....	....
7.....	2060	13.0	....	0.46	....	....	....	....	....	....
8.....	1840	11.1	....	0.42	....	....	....	....	....	....
9.....	1770	10.3	....	0.41	....	....	....	....	....	....

Day of Disease.	Volume c.c.	Urine Nitrogen as						Per Cent. Total N.		
		Total.	NH_3.	Kreatinin.	Kreatin.	Uric Acid.	"Rest."	Urea.	NH_3.	"Rest."
				Period VII.						
10	2310	9.7	....	0.43	....	....	....	....	....	....
11	2220	7.3	....	0.41	....	....	....	....	....	....
12	3400	7.2	....	0.45	....	....	....	....	....	....
13	2370	5.4	....	0.50	....	....	....	....	....	....
14	2360	6.5	....	0.50	....	....	....	....	....	....
15	2010	6.9	....	0.41	....	....	....	....	....	....
16	3300	....	....	0.45	....	....	....	....	....	....
17	2630	7.7	....	0.42	....	....	....	....	....	....
18	3010	7.3	....	0.43	....	....	....	....	....	....
19	2750	7.5	....	0.46	....	....	....	....	....	....

TABLE 23.—PATIENT 6, L—D: DAILY NITROGEN BALANCE.

Day of Disease.	Food.				Excretion N.	Nitrogen Balance.
	Total Calories.	Cal. Per Kg. Total.	Cal. Per Kg. From C. H.	Nitrogen.		
		Period I.				
17	1425	22	6	9.3	17.9	— 8.6
18	1545	24	6	10.1	....	.....
19	1545	24	6	10.1	19.6	— 9.5
20	1545	24	6	10.1	17.3	— 7.2
Normal Temperature.		Period II.				
1	1985	31	11	9.2	16.9	— 7.7
2	2750	44	20	9.4	13.0	— 3.6
3	3470	55	26	11.3	12.6	— 1.3
4	2940	47	25	9.3	11.6	— 2.3
5	3620	58	26	11.5	9.8	+ 1.7
6	3210	51	26	10.7	10.7	+ 0.0
		Period III.				
7	3060	48	23	11.7	....	.....
8	2575	41	19	10.4	10.6	— 0.2
Relapse.						
1	4320	68	32	16.1	13.8	+ 2.3
2	3670	57	29	14.1	13.0	+ 1.1
3	3930	61	30	11.0	12.0	— 1.0
4	3750	59	30	13.2	12.5	+ 0.7
		Period IV.				
5	3560	56	29	12.1	14.7	— 2.6
6	3510	55	25	10.2	14.0	— 3.8
7	3620	57	20	12.6	16.5	— 3.9
8	3310	52	12	10.3	15.2	— 4.9
9	3620	57	18	8.7	14.8	— 6.1
		Period V.				
10	4540	71	28	13.9	12.2	+ 1.7
11	4750	74	41	13.7	10.3	+ 3.4
12	5250	82	48	13.7	9.8	+ 3.9
13	5230	82	48	13.2	9.7	+ 3.5
Convalesecnce.						
1	5250	82	48	13.7	9.7	+ 4.0
2	4630	72	39	13.7	9.5	+ 4.2
3	5250	82	48	13.7	8.9	+ 4.8
4	5100	79	48	13.7	....	.....
		Period VI.				
5	2420	37	4	13.7	11.1	+ 2.6
6	2420	37	4	13.7	12.4	+ 1.3
7	2170	34	4	13.9	14.5	— 0.6
8	2420	37	4	13.7	12.6	+ 1.1
9	2420	37	4	13.7	11.8	+ 1.9
		Period VII.				
10	4630	70	38	13.7	11.7	+ 2.0
11	5250	79	46	13.7	9.3	+ 4.4
12	5120	76	44	13.7	9.2	+ 4.5
13	5100	76	45	13.0	7.3	+ 5.7
14	4220	62	30	13.7	8.5	+ 5.2
15	3900	58	26	13.7	8.9	+ 4.8
16	3900	58	26	13.7	....	.....
17	3900	58	26	13.7	9.7	+ 4.0
18	3760	55	25	12.8	9.2	+ 3.6
19	3900	58	26	13.7	9.3	+ 4.4

TABLE 24.—PATIENT 6, L.—D: AVERAGES FROM PERIODS.
Figures given are for 24 hours.

No. of Days.	Range of Maximum Temp. F. During Period.	Food. Cal. Per Kg. Total.	Fat.	C. H.	Nitrogen, Gm.	Excretion N.	Balance N.	Urine. Kreatinin N.	Kreatin N.	NH_3 N. Gm.	NH_3 N. Per Cent. of Total N.	"Rest" N. Gm.	"Rest" N. Per Cent. of Total N.	Uric Acid N.	Xanthin Bases Mg. Xanthin.	Kreatinin Coef.
							Period I.									
4	102.2– 99.4	24	13	6	10.0	18.3	—8.3	0.43	0.11	1.00	6.0	0.67	4.0	0.27	42‡	6.7
							Period II.									
6	Normal	51	22	24	10.4	11.5*	—1.1	0.38	0.03	0.65	6.5	0.54	5.4	0.14	48‡	6.0
							Period III.									
6	99.6–103.0	58	25	28	12.9	12.3	+0.6	0.51	0.06	0.81	7.8	0.58	5.6	0.14	..	8.0
							Period IV.									
5	103.4–102.0	55	30	21	10.8	14.6	—3.8	0.51	0.02	1.04†	7.7	0.85†	6.4	0.20	52‡	8.0
							Period V.									
8	101.6– 99.2	78	29	43	13.7	9.9	+3.8	0.40	0.00	....	...	....	...	0.16‡	..	6.2
							Period VI.									
5	Normal	37	27	4	13.7	12.5	+1.2	0.41	....	....	...	....	...	0.15‡	..	6.4
							Period VII.									
10	Normal	64	26	33	13.6	9.3	+4.3	0.45	....	....	...	....	...	0.13‡	..	6.7

* First day of period excluded from average.
† Average of first three days of period.
‡ Determination made in "composite" urines.

TABLE 25.—PATIENT 7, G—T: DAILY FOOD.

Day of Disease.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose. Gm.	Butter. Gm.	Toast. Gm.	Beef Extract. Gm.	Somatose. Gm.	Whisky. c.c.	Protein. Gm.	Fat. Gm.	C. H. Gm.
					Period I.							
30	640	150	..	270	...	...	..	..	..	24.1	77	306
31	400	100	..	600	...	...	..	..	60	15.2	50	623
32	1500	...	..	330	...	...	..	..	50	49.5	75	405
33	1500	...	..	120	...	...	..	..	90	49.5	75	285
34	2000	...	..	...	...	...	..	..	90	66.0	100	100
35	1800	60	..	185	...	...	..	..	90	60.6	108	277
36	2000	...	..	...	...	...	..	..	90	66.0	100	100
37	2000	...	..	...	...	...	..	..	90	66.0	100	100
38	1230	120	..	345	...	...	..	..	75	43.0	97	410
Average (excluding first two days)										57.2	93	240
					Period II.							
39	1350	150	..	520	...	...	..	..	75	47.0	112	592
40	1435	60	..	505	...	...	..	..	90	48.5	90	578
41	1440	60	..	493	...	...	..	..	90	48.7	90	567
Average										48.0	97	579
					Period III.							
42	1350	60	..	455	...	...	..	60	90	94.0	85	526
43	1110	60	..	410	...	...	..	60	90	84.5	73	467
44	1110	60	..	290	...	...	..	60	90	84.5	73	347
Average										87.7	77	447
					Period IV.							
45	1470	60	1	345	...	...	..	..	90	57.0	97	420
46	1470	60	2	345	...	...	..	..	90	64.2	102	420
47	1410	60	2	305	...	...	..	..	90	62.0	99	377
48	1410	60	2	365	...	...	..	..	90	62.0	99	437
Average (excluding first day of period)										62.7	100	411
					Period V.							
49	2190	...	..	...	...	...	..	..	90	72.3	110	110
50	2190	...	..	...	...	...	..	..	90	72.3	110	110
51	2190	...	..	...	...	...	..	..	90	72.3	110	110
Average										72.3	110	110

Day of Disease.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose. Gm.	Butter. Gm.	Toast. Gm.	Beef Extract. Gm.	Somatose. Gm.	Whisky. c.c.	Protein. Gm.	Fat. Gm.	C. H. Gm.
					Period VI.							
52	2400	...	..	...	...	...	60	..	..	79.2*	120	120
53	1920	...	..	...	...	...	60	..	..	63.3*	96	96
Average										71.2*	108	108
					Period VII.							
54	795	390	4	195	...	...	..	..	..	62.8	178	246
55	1080	330	4	360	...	30	..	..	..	74.4	174	442
56	1320	270	4	320	30	60	..	..	..	84.4	194	427
57	1290	270	5	310	...	...	..	..	..	84.0	172	380
58	1140	270	4	280	...	...	..	..	..	71.8	159	345
Average (excluding first day of period)										78.6	175	398
					Period VIII.							
59	1440	300	2	325	...	...	..	..	..	68.0	173	406
60	1380	600	2	190	...	...	..	..	..	72.0	260	277
61	1260	480	2	300	...	...	..	..	..	65.5	218	377
62	1260	480	2	240	...	...	..	..	..	65.5	218	377
Average										67.8	216	344
					Period IX.							
63	520	240	1	180	...	...	..	..	..	29.0	103	213
64	480	240	..	...	...	...	51	..	..	20.6	96	171
65	1020	120	..	140	...	...	..	..	..	36.0	87	195
66	1590	90	..	160	...	...	..	..	..	54.3	107	242
67	1820	120	..	160	...	...	..	..	..	62.4	127	255
68	2160	...	..	180	...	...	..	..	..	71.4	108	288
69	2160	...	..	180	...	...	..	..	..	71.4	108	288
70	2160	...	..	180	...	...	..	..	..	71.4	108	288
Average (last three days of period)										71.4	108	288
					Period X.							
71	2160	...	1	180	...	...	..	..	..	78.5	113	288
72	2160	...	2	155	...	...	..	..	..	85.7	119	263
73	2160	...	2	150	...	...	..	..	..	85.7	119	258
74	2160	...	2	180	...	...	..	..	..	85.7	119	288
75	2160	...	2	180	...	...	..	..	..	85.7	119	288
76	2160	...	2	315	...	...	..	..	..	85.7	119	421
Average										84.5	118	301

* Does not include nitrogen of beef extract.

Day of Disease.	Milk. c.c.	Cream. c.c.	Eggs.	Lactose. Gm.	Butter. Gm.	Toast. Gm.	Beef Extract. Gm.	Somatose. Gm.	Whisky. c.c.	Protein. Gm.	Fat. Gm.	C. H. Gm.
					Period XI.							
77	2160	180	3	405	8	30	..	..	..	99.8	190	536
78	2040	255	4.5	385	16	...	..	..	..	104.8	225	495
79	1920	240	4	360	16	...	..	..	..	97.0	210	463
80	2160	270	5	540	76	60	..	..	..	119.3	291	692
81	1920	240	4	480	61	60	..	..	..	103.6	249	619
82	2160	180	5	180	106	60	..	..	..	117.5	288	329
83	2160	210	5	540	106	105	..	..	..	123.1	297	717
84	2400	300	5	540	136	90	..	..	..	131.2	362	723
Average										112.0	264	572
					Period XII.							
85	2160	270	5	...	136	90	..	..	..	122.6	332	170
86	2400	300	5	...	135	120	..	..	..	134.4	352	201
87	2400	210	5	...	103	120	..	..	..	132.6	298	198
88	2400	300	5	...	111	120	..	..	..	134.4	332	191
89	1680	240	5	330	111	150	..	..	..	112.8	278	511
Average										127.4	318	254
					Period XIII.							
90	2400	330	5	520	111	150	..	60	..	183.0	320	740
91	2400	300	5	600	111	150	..	60	..	182.4	311	820
92	2400	300	5	600	111	150	..	60	..	182.4	311	820
93	2160	270	5	600	87	120	..	60	..	172.5	290	788
94	2160	270	5	600	111	150	..	60	..	176.0	310	806
Average										179.0	317	795
					Period XIV.							
95	2400	300	5	...	111	150	..	60	..	184.0	331	219
96	2400	300	5	...	111	150	..	60	..	184.0	331	219
97	2400	300	5	...	111	150	..	30	..	161.0	331	219
Average										176.0	331	219
					Period XV.							
98	2400	300	5	...	111	150	..	..	..	127.7	331	219
99	2400	300	5	...	111	150	..	..	..	127.7	331	219
100	2400	300	5	...	111	120	..	..	..	124.4	331	201
101	2160	300	5	...	120	165	..	..	..	131.4	327	216
Average										127.8	330	214

quickly stopped when the food was increased to 78 calories per kg. and 13.7 gm. nitrogen, the average of the next period (V).

During each of the eight days of this period (V), on three of which the temperature was above normal, the subject showed a plus balance of nitrogen, the average being 3.8 gm. Practically no kreatin was excreted.

For the following five days of normal temperature the greater part of the carbohydrate was withdrawn from the food, which was otherwise the same as in Period V, and represented 13.7 gm. nitrogen and 37 calories per kg. The excessive endogenous katabolism of protein observed in earlier periods had ceased and this diet was more than sufficient for equilibrium, the subject gaining 1.2 gm. nitrogen per day.

In the last period (VII) much carbohydrate was again added and an average plus balance of 4.3 gm. nitrogen was found. Carbohydrate equivalent to about 30 calories per kg. added to the food caused an increased retention of 3.1 gm. nitrogen (4.3-1.2) per day for ten days.

Patient 7—G—t, male, 38 years of age, tinsmith, admitted on the twenty-first day of the disease, claimed to have lost 15 pounds, but looked well-nourished. Illness very severe. Duration of fever forty-seven days, followed by a relapse of twenty-seven days. Complicated by serofibrinous pleurisy, cholecystitis with jaundice, and several slight intestinal hemorrhages. Sputum bloody but no tubercle bacilli could be found.

The experiment with this patient is the longest of this series. Our observations began on the thirteenth day of the disease, which was twenty days before the temperature remained normal for the first time, and continued for seventy-two days, on forty-seven of which fever was present. In spite of this long and very severe illness, the patient weighed about 2 kg. more at the end than at the start of the experiment. According to the sum of the daily balances of nitrogen, there was during the experiment a total loss of about 150 gm. (allowing 20 gm. for the days on which the urine was lost) and a total gain of 243 gm., giving a net gain of about 93 gm. of nitrogen. This is the equivalent of about 2.9 kg. of muscle tissue (33).

The seventy-two days of the experiment are divided into fifteen periods, the average results of which are given in Table 28. The daily data are given in Tables 25, 26 and 27.

During the time of Periods I to IV, and VII to XI, inclusive, the patient had a fever temperature, while in the remaining periods the temperature was practically normal. In Period I there was an average daily loss of 7.7 gm. nitrogen (excluding the first two days, when the protein intake was very low) with food of an average value of 32 cal. per kg. and 9.2 gm. nitrogen. During the next three days (II) the food was increased by the equivalent of 21 cal. per kg. in the form of carbohydrate, and the nitrogen loss was decreased by 5.5 gm. per day. This result is probably in part due to a lowered intensity of the katabolic processes coincident with the fall in temperature, because in the two following periods (III and IV) a slight plus balance was obtained, though the food was of less caloric value (but of higher protein value) than in Period II.

In Periods V and VI the temperature was about normal and the protein katabolism was not markedly abnormal; minus balances of 0.6 and 0.7 gm. nitrogen were obtained with food equivalent to 28 and 27 cal. per kg.

Table 26.—Patient 7, G—T: Daily Analysis of Urine.*

Day of Disease.	Volume c.c.	Nitrogen. Total.	Kreatinin.	Kreatin.	Uric Acid.
	Period I.				
30	750	16.0	0.50	0.10	0.25
31	950	18.3	0.63	0.15	0.33
32	1570	12.0	0.51	0.01	0.28
33	2450	16.3	0.54	0.13	0.32
34	1970	16.3	0.50	0.19	0.23
35	1050	14.3	0.39	....	....
36	1590	15.5	0.37	0.17	0.24
37	1490	15.3	0.43	0.11	0.23
38	1490	15.3	0.43	0.11	0.23
	Period II.				
39	740	8.9	0.36	0.01	0.22
40	1000	9.0	0.50	0.09	....
41	800	8.4	0.45	0.04	....
	Period III (Somatose).				
42	920	9.1	0.39	0.07	....
43	1860	10.5	0.46	0.04	....
44	1620	11.1	0.41	0.07	....

Day of Disease.	Volume c.c.	Nitrogen. Total.	Kreatinin.	Kreatin.	Uric Acid.
		Period IV.			
45	1920	11.0	0.43	0.05	....
46	1670	8.8	0.41	0.00	....
47	1740	8.3	0.41	0.02	....
48	1430	7.9	0.36	0.05	....
		Period V.			
49	2060	8.8	0.38	0.02	....
50	2060	10.2	0.39	0.03	....
51	1940	10.8	0.41	0.02	0.11
		Period VI (Meat Extract).			
52	2135	12.3	0.72	0.21	0.30
53	2040	15.0	0.86	0.40	0.49
		Period VII.			
54	1580	10.4	0.40	0.01	0.19
55	1320	7.3	0.39	0.00	....
56	1900	7.4	0.43	0.00	....
57	1950	7.7	0.47	0.00	....
58	1880	7.7	0.47	....	....
		Period VIII.			
59	1360	5.8	0.36	0.06	....
60	2650	6.9	0.40	0.12	....
61	2040	6.9	0.48	....	....
62	2340	7.8	0.53	....	....
		Period IX.			
63	1870	8.4	0.58	....	....
64	2000	14.6	0.84	Meat Extract	....
65	1380	14.9	0.55	....	....
66 Urine lost.					
67 Urine lost.					
68	860	12.7	0.60	....	....
69 Urine lost.					
70	1160	13.7	0.52	....	....
		Period X.			
71	1330	12.5	0.50	....	....
72	1300	12.3	0.47	....	....
73	1320	11.8	0.56	....	....
74	1200	11.7	0.56	....	....
75	1400	10.1	0.53	....	....
76	1600	11.0	0.48	....	....
		Period XI.			
77	1440	9.8	0.49	....	....
78	1660	8.4	0.41	....	....
79	1860	8.8	0.39	....	....
80	1560	8.0	0.39	....	....
81	1660	9.3	0.41	....	....
82	1580	7.3	0.36	....	....
83	1680	8.6	0.42	....	....
84	1830	8.4	0.36	0.02	....
		Period XII.			
85	2360	9.3	0.37	0.02	....
86	2140	10.7	0.36	0.02	....
87	2225	11.4	0.34	....	....
88	1860	11.2	0.35	....	....
89	1700	10.1	0.38	....	....
		Period XIII (Somatose).			
90	1860	8.6	0.36	....	....
91	1600	8.3	0.37	....	....
92	2150	8.5	0.35	....	....
93	2700	8.3	0.35	....	....
94	2660	9.6	0.37	....	....
		Period XIV (Somatose).			
95	3040	11.9	0.44	0.00	....
96	2410	14.7	0.41	0.00	....
97	2210	15.3	0.39	0.00	....
		Period XV.			
98	2140	14.0	0.35	0.00	....
99	2250	13.9	0.39	0.00	....
100	1620	11.5	0.33	0.03	....
101	2000	13.6	0.38	0.02	....

* During Period VI, and on second day of Period IX, subject was given meat extract. During Periods III, XIII and XIV, the food contained "somatose."

TABLE 27.—PATIENT 7, G—T: DAILY TEMPERATURE AND NITROGEN BALANCE.*

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Total Cal.	Cal. Per Kg. Total.	Cal. Per Kg. C. H.	Nitrogen Balance. Intake.	Nitrogen Balance. Excretion.	Nitrogen Balance. Balance.
				Period I.					
30	67.0	105.0	103.2	2065	31	19	3.8	16.6	—12.8
31	....	104.0	103.0	3085	46	38	2.4	18.7	—16.3
32	67.4	104.2	102.6	2570	38	25	7.8	13.2	— 5.4
33	....	104.0	103.2	2075	31	17	7.8	17.5	— 9.7
34	....	104.8	102.0	1610	24	6	10.5	17.9	— 7.4
35	65.6	104.0	103.2	2390	36	18	9.7	15.7	— 6.0
36	....	103.6	102.0	1610	24	6	10.5	17.1	— 6.6
37	....	103.4	102.2	1610	24	6	10.5	16.6	— 7.9
38	....	103.0	101.4	2760	42	26	6.9	16.6	— 7.9
				Period II.					
39	65.0	103.4	100.4	3660	56	37	7.5	10.0	— 2.5
40	....	103.2	100.4	3405	52	36	7.7	10.1	— 2.4
41	....	102.8	100.0	3350	52	36	7.8	9.6	— 1.8
				Period III.					
42	64.5	102.6	100.4	3330	52	33	15.0	(11.3)	(+ 3.7)
43	....	103.2	99.6	2950	46	30	13.5	12.5	+ 1.0
44	63.5	102.8	99.8	2450	38	22	13.5	13.1	+ 0.4
				Period IV.					
45	63.3	101.4	99.4	2860	45	27	9.1	(12.4)	(— 3.3)
46	....	102.2	98.8	2920	46	27	10.3	10.3	+ 0.0
47	63.5	101.2	98.8	2720	43	24	9.9	9.8	+ 0.1
48	....	100.6	98.6	2960	47	28	9.9	9.4	+ 0.5
				Period V.					
49	64.0	100.2	98.4	1765	28	7	11.5	(10.5)	(+ 1.0)
50	....	100.0	97.6	1765	28	7	11.5	11.9	— 0.4
51	62.5	100.4	98.4	1765	28	7	11.5	12.3	— 0.8
				Period VI.					
52	....	100.0	98.2	1930	31	8	18.0	(15.0)	(+ 3.0)
53	....	99.8	98.6	1540	24	6	15.4	17.3	— 1.9
				Period VII.					
54	....	100.4	98.8	2920	46	16	10.0	11.9	— 1.9
55	....	101.6	99.2	3740	60	29	11.9	9.1	+ 2.8
56	....	102.6	99.6	3900	62	28	13.5	9.6	+ 3.9
57	....	103.8	100.0	3500	55	25	13.4	9.9	+ 3.5
58	....	102.6	99.2	3190	50	22	11.5	9.4	+ 2.1
				Period VIII.					
59	....	101.8	98.8	3550	56	26	10.9	7.6	+ 3.3
60	....	101.8	99.4	3850	60	18	11.5	8.7	+ 2.8
61	....	102.6	99.8	3850	60	24	10.5	8.7	+ 1.8
62	....	103.4	100.6	3600	56	20	10.5	9.6	+ 0.9
				Period IX.					
63	....	104.4	102.4	1950	30	14	4.6	10.2	— 5.6
64	....	104.8	103.2	1680	26	11	8.1	16.4	— 8.3
65	....	104.6	103.6	1760	27	12	5.8	16.7	—10.9
66	....	104.8	103.4	2210	34	15	8.7	....	.....
67	65.1	104.2	102.8	2480	38	16	10.0	....	.....
68	....	104.8	102.8	2480	38	18	11.4	14.5	— 3.1
69	....	104.8	102.8	2480	38	18	11.4	....	.....
70	64.2	104.2	102.8	2480	38	18	11.4	15.5	— 4.1
				Period X.					
71	....	103.6	101.8	2550	40	18	12.5	14.4	— 1.9
72	....	104.0	102.4	2530	39	17	13.7	14.4	— 0.7
73	....	103.2	101.2	2520	39	16	13.7	13.9	— 0.2
74	....	102.6	101.4	2740	43	18	13.7	13.8	— 0.1
75	....	102.6	101.4	2740	43	18	13.7	12.2	+ 1.5
76	....	102.5	100.2	3180	49	26	13.7	13.1	+ 0.6
				Period XI.					
77	....	102.4	100.4	4373	68	34	16.0	12.2	+ 3.8
78	....	102.0	99.5	4546	71	31	16.7	10.9	+ 5.8
79	....	101.0	99.0	4253	66	29	15.5	11.1	+ 4.4
80	....	100.8	98.6	6040	94	44	19.1	10.9	+ 8.2
81	....	101.4	98.4	5280	82	39	16.6	11.8	+ 4.8
82	....	100.0	98.6	4510	70	21	18.8	10.1	+ 8.7
83	....	100.4	98.4	6210	96	46	19.7	11.6	+ 8.1
84	....	100.2	98.6	6860	106	46	21.0	11.6	+ 9.4

Day of Disease.	Wt. Kg.	Temp. F. High.	Temp. F. Low.	Total Cal.	Cal. Per Kg. Total.	Cal. Per Kg. C. H.	Nitrogen Balance. Intake.	Nitrogen Balance. Excretion.	Nitrogen Balance. Balance.
			Period XII.						
85	....	99.8	98.6	4290	67	11	19.6	12.2	+ 7.4
86	....	99.8	98.4	4645	72	13	21.5	13.9	+ 7.6
87	....	99.6	98.4	4126	64	13	21.2	14.6	+ 6.6
88	....	99.6	98.4	4425	69	12	21.5	14.4	+ 7.1
89	64.6	100.2	98.6	5140	80	32	17.9	12.8	+ 5.1
			Period XIII.						
90	....	100.4	98.6	6760	104	47	29.3	13.0	+16.3
91	....	99.8	98.8	7000	107	52	29.2	12.7	+16.5
92	65.0	99.6	98.4	7000	107	52	29.2	12.9	+16.3
93	....	100.4	99.8	6640	102	50	27.6	12.4	+15.2
94	....	100.2	99.4	6900	106	51	28.2	13.8	+14.4
			Period XIV.						
95	....	100.6	99.0	4730	71	13	29.4	16.3	(+13.1)
96	....	100.4	99.0	4730	71	13	29.4	19.0	(+10.4)
97	68.2	100.2	98.6	4640	68	13	25.8	19.2	(+ 6.6)
			Period XV.						
98	68.7	99.8	98.2	4500	65	12	20.4	17.1	+ 3.3
99	....	99.8	98.4	4500	65	12	20.4	17.0	+ 3.4
100	....	99.4	98.4	4410	64	12	19.9	14.5	+ 5.4
101	68.8	100.0	98.4	4460	65	12	21.0	16.7	+ 4.3

* In Period VIII, the feces contained 1.8 gm. N. per day. In other periods "excretion"=total N. of urine + 15 per cent. of food N.

In Period VII, coincident with the beginning of a relapse, the carbohydrate food was again increased and, during the next nine days of fever (VII and VIII), the subject gained nitrogen each day, the diet equaling 56 and 58 cal. per kg. and 12.6-10.8 gm. nitrogen. Here, again, it seems very clear that we wholly prevented any febrile loss of body protein.

In Period IX the patient's condition became more serious and we were able to give only a moderate amount of food, 38 cal. per kg. and less. The consequent great disproportion between the decreased food-supply and the probably increased demand for energy or increased intensity of the katabolic processes resulted in very considerable losses of body nitrogen (3 to 10 gm. daily). That the loss was not even greater seems surprising, and is probably to be explained by the known tendency of the organism to react less violently to such a stimulus in the later stages of a long illness.

This same tendency probably explains the fact that during the next period (X), with the temperaure still above normal, nitrogen equilibrium was attained on almost the same diet.

On further increasing the value of the food to 82 cal. per kg. (XI) there was an average plus balance of 6.6 gm. nitrogen per day, though the maximum temperature on four days was above 101 F.

During the remainder of the experiment the temperature was normal and the excessive katabolism observed during the febrile reaction had given place to the increased anabolism characteristic of convalescence. Food of high protein content and equivalent to 70 (*XII*), 105 (*XII*), 70 (*XIV*) *and* 65 (*XV*) *cal. per kg. resulted in the large average daily plus balances of* 6.8, 15.7, 8.7 *and* 4.1 *gm. nitrogen.*

A comparison of Periods XIII and XIV shows the great value of carbohydrate in assisting the gain of protein in convalescence, which is not wholly in accord with the idea of Benedict and Surànyi, that the nitrogen retention in convalescence is largely independent of the fuel value of the food.

A comparison of Periods II and VIII again illustrates the importance of the intensity of the katabolic process in determining the degree of sparing of body protein to be accomplished by any diet. The intensity of the katabolism does not always go parallel to the temperature, as has been pointed out by Kraus and others. In both of the above periods the maximum temperature was about the same, and the food differed only slightly.

Food.	Cal. Per. Kg. Total.	Cal. Per. Kg. Fat.	Cal. Per. Kg. C. H.	N. Gm.	N. Bal.
Period II	54	14	36	7.7	—2.2
Period VIII	58	31	22	10.8	+2.1

TABLE 28.—PATIENT 7, G—T: AVERAGES OF PERIODS.
Figures given for 24 hours.

			Food.						Urine.										
			Cal. Per Kg.									NH_3 N.			"Rest" N.				
	No. of Days.	Range of Maximum Temp. During Period.	Total.	From Fat.	From C. H.	Nitrogen Gm.	Excretion N.[13] Gm.	Nitrogen Balance. Gm.	Total Nitrogen.	Kreatinin N.	Kreatin N.	Gm.[1]	Per Cent. Total N.	Uric Acid N.	Gm.[1]	Per Cent. Total N.	Urea. Per Cent. Total N.[1]	Xanthin Bases. Gm. Xanthin.[1]	Kreatinin Coef.
Period I.....	9	105.0–103.0	32	13	15	9.2	16.9	— 7.7	15.5	0.48	0.12	1.13	7.1	0.25	1.46	9.2	77.9	0.040	7.3
Period II.....	3	103.4–102.8	54	14	36	7.7	9.9	— 2.2 (+ 0.4)	8.8	0.44	0.04	0.82	9.6	0.24[1]	1.02	11.6	69.9	.....	6.8
Period III.....	3	103.2–102.6	45	11	29	14.0	12.8[2]	+ 1.2	10.8	0.42	0.06	....	....	0.26[1]	1.00	9.8	....	0.086	6.5
Period IV[4]....	4	102.2–100.6	45	15	27	10.0	9.8	+ 0.2	8.3	0.39	0.02	0.59	7.2	0.20[1]	0.88	10.7	74.5	0.063	6.1
Period V.....	3	100.4–100.0	28	16	7	11.5	12.2[3]	— 0.7	10.5	0.40	0.02	....	....	0.11	....	....	....	.....	6.3
Period VI[5]....	2	100.0– 99.8	27	16	7	16.7[6]	17.3[7]	— 0.6	15.0	0.86	0.40	....	....	0.49	Beef Extract.			0.064	...
Period VII[4]...	5	100.4–103.8	56	25	25	12.6	9.4	+ 3.2	7.5	0.44	0.00	0.58	7.2	0.17[1]	0.98	12.1	72.7	0.072	6.9
Period VIII...	4	101.8–103.4	58	31	22	10.8	8.7	+ 2.1	6.9	0.44	....	0.75	11.0	0.15[1]	0.64	9.4	70.0	0.079	6.9
Period IX.....	8	104.2–104.8	38[8]	16[8]	18[8]	11.4[8]	15.0[9]	— 3.6[9]	12.9[10]	0.56[11]	....	1.02	8.0	0.33[1]	1.50	11.5	73.3	0.066	8.7
Period X.....	6	104.0–102.4	42	17	19	13.5	13.6	— 0.1	11.6	0.51	....	1.07	9.2	0.30[1]	0.96	8.5	72.4	0.071	8.0
Period XI.....	8	102.4–100.0	82	38	37	17.9	11.3	+ 6.6	8.6	0.40	....	0.77	9.0	0.24[1]	1.07	12.4	72.5	0.055	6.2
Period XII.....	5	99.6–100.2	70	46	16	20.4	13.6	+ 6.8	10.5	0.36	....	0.67	6.4	0.24[1]	0.79	7.5	80.4	0.050	5.6
Period XIII...	5	100.4– 99.6	105	45	50	28.7	13.0	+15.7	8.7	0.36	....	0.60	6.9	0.22[1]	0.72	8.3	78.1	0.042	5.5
Period XIV....	3	100.6–100.2	70	45	13	28.2	19.5[12]	+ 8.7	15.3	0.41	0.00	....	....	0.23[1]	....	....	....	.....	6.0
												0.55	4.0	....	....	....	....	0.051	...
Period XV....	4	100.0– 99.2	65	45	12	20.4	16.3	+ 4.1	13.3	0.36	0.01	....	....	0.24[1]	....	....	....	.....	5.2

1. Determined in "composite urines" representing periods.
2. First two days of period excluded from averages for nitrogen balance and food.
3. First day of period excluded from average for excretion.
4. First day of period excluded from averages for nitrogen balance and food.
5. Beef extract period. Note high kreatinin, kreatin and uric acid.
6. 5.3 gm. of this N. was in form of beef extract.
7. Excretion of last day of period. 60 gm. beef extract were given on each of the two days.
8. Average of last three days.
9. Average of two of the last three days—urine of other day lost. Patient at times incontinent.
10. Average of five days of period. Urine of other days lost.
11. Average of four days—beef extract day excluded.
12. Excretion of last day used for nitrogen balance. Total N. of urine (15.3 gm.) + 15 per cent. of food-nitrogen (4.2 gm.).
13. In Period VIII the feces were collected and found to contain 1.8 gm. N. per day. "Excretion" of other periods = total N. of urine + 15 per cent. of food-nitrogen.

TABLE 29.—PATIENT 8, P—S: DAILY FOOD AND ANALYSES OF URINE.
Insufficient food-supply throughout. Great loss of body protein. Great emaciation.

Day of Disease.	Temp. F.		Urine.										Remarks.
										Per Cent. of Total N.			
	High.	Low.	Volume c.c.	Total N.	NH_3 N.	Kreatinin N.	Kreatin N.	Uric Acid N.	"Rest" N.	Urea.	NH_3.	Rest.	
12	104.0	103.0	1280	22.7	1.61	0.54	0.71	0.17	1.56	80.0	7.1	6.9	*
13	103.5	102.4	1280	22.7	1.61	0.54	0.71	0.17	1.56	80.0	7.1	6.9	*
14	103.4	102.0	1350	22.4	1.80	0.54	0.67	0.19	1.07	81.0	8.0	4.8	*
15	103.5	102.0	860	....	....	0.35	0.34	0.11	....	....	7.9	....	
16	103.4	102.0	1240	18.7	1.65	0.52	0.48	0.19	1.62	76.3	8.8	8.7	*
17	103.4	101.0	1040	14.8	1.38	0.43	0.31	0.13	1.29	76.1	9.3	8.7	
18	104.4	99.0	1300	20.8	1.84	0.54	0.57	0.21	1.72	76.7	8.9	8.3	*
19	103.0	102.0	....	....	....	....	....	....	....	....	....	....	
20	103.0	103.0	950	13.8	0.07	0.37	0.38	0.11	1.24	77.0	7.8	9.0	
21	103.6	101.0	1140	14.7	1.44	0.43	0.37	0.07	1.32	75.3	9.8	9.0	
22	104.0	102.4	1150	15.9	1.47	0.49	0.35	0.11	....	....	9.2	....	*
23	104.0	100.0	....	....	....	....	....	....	....	....	....	....	
24	105.6	102.8	920	10.2	1.10	0.35	0.22	0.08	0.94	73.7	10.8	9.2	
25	104.4	103.4	....	....	....	....	....	....	....	....	....	....	
26	103.6	101.0	....	11.7?	1.44	0.51	0.17	0.13	1.62	66.9	12.4	13.9	*
27	103.4	102.0	....	8.0?	....	0.50	0.18	0.12	1.62	61.2	14.1	16.5	*
28	102.6	101.0	....	....	....	....	....	....	....	....	....	....	
29	103.0	100.0	....	....	....	....	....	....	....	....	....	....	
30	103.0	100.6	900	15.4	1.17	0.31	0.26	0.08	0.87	82.5	7.6	5.6	
31	103.0	101.0	1380	18.5	1.36	0.42	0.38	0.14	1.36	80.2	7.4	7.4	*
32	102.6	99.6	....	....	....	....	....	....	....	....	....	....	
33	102.6	99.6	1500	13.9	1.30	0.26	0.20	0.13	0.75	81.4	9.3	5.4	
34	103.6	101.8	2180	13.7	....	....	....	....	....	....	....	....	
35	102.0	100.4	1800	12.7	1.02	0.18	0.12	0.10	1.09	80.4	8.0	8.6	
36	103.0	99.0	800	8.8	0.61	0.18	0.15	0.07	1.15	75.6	6.9	13.1	
37	103.0	100.0	1800	....	....	....	....	....	....	....	....	....	
38	102.4	99.0	1960	....	....	0.30	....	....	....	....	....	....	
39	102.4	99.0	....	....	....	....	....	....	....	....	6.0	11.0	
40	102.4	99.6	1400	14.8	0.84	0.37	0.02	0.12	1.66	....	5.7	11.2	*
41	103.0	99.6	1320	14.2	0.66	0.42	....	0.12	1.17	83.4	4.6	8.2	*
42	103.0	101.0	1580	12.3	0.80	....	....	0.07	....	....	....	....	
43	103.4	100.6	1260	10.9	0.68	0.25	0.03	0.09	0.89	81.6	6.2	8.2	
44	104.4	100.4	750	10.5	0.74	0.28	0.00	0.08	1.04	79.6	7.0	9.9	*
45	103.8	101.6	540	....	....	....	....	....	....	....	7.9	9.3	
46	102.4	100.4	630	8.5	0.60	0.23	0.07	0.06	0.72	80.1	7.0	8.5	
47	104.4	100.4	520	6.0	....	....	0.03	0.04	0.56	80.3	8.1	8.3	
48	104.0	102.0	1360	14.7	1.01	0.27	....	0.07	1.34	81.8	6.8	9.1	*
49	103.0	100.0	620	7.2	....	....	0.00	0.05	....	....	3.4	8.8	†
50	103.0	101.0	730	9.6	0.71	0.27	....	0.07	0.85	80.3	7.3	8.8	*
51	103.0	100.0	390	....	....	....	....	0.04	....	....	8.2	7.8	
52	104.4	101.0	570	....	....	....	....	0.09	....	....	7.4	8.9	
53	103.0	101.0	570	10.0	0.73	0.28	....	0.09	....	....	7.3	....	*
54	102.4	100.0	930	10.0	0.73	0.28	....	0.09	....	....	7.3	....	*
55	103.0	100.0	1180	12.7	....	0.22	....	....	....	....	....	....	*
56	102.4	100.0	670	6.8	....	0.22	....	0.06	....	....	....	....	
57	103.0	99.0	890	9.9	....	....	....	....	....	....	....	....	
58	100.8	98.4	....	....	....	....	....	....	....	....	....	....	

* Many of the urines of this patient were incomplete; those which are known to be complete are marked with a *.
† Wt. 42 Kg.

TABLE 30.—PATIENT 9, O—Y: DAILY FOOD AND ANALYSES OF URINE.
Weight about 50 Kg.

Average Daily Food and Nitrogen Balance.	Day of Disease.	Temp. F. High.	Temp. F. Low.	Urine. Volume c.c.	Urine. Total N.	Urine. NH_3 N.	Urine. Kreatinin N.	Urine. Kreatin N.	Urine. Uric Acid N.	Urine. "Rest" N.	Per Cent. of Total N. Urea.	Per Cent. of Total N. NH_3.	Per Cent. of Total N. Rest.
Period I.													
34 Cal. per kg. 11.1 gm. N. Bal. = — 6.7	9	105.0	103.0	2170	13.9	11.3	0.45	....	0.18	1.04	79.1	8.2	7.5
	10	104.6	102.0	3110	28.4	....	0.73	0.28	0.14	2.07	....	....	9.5
	11	104.0	102.4	1200	13.1	0.76	0.36	0.14	0.14	0.77	83.5	5.6	5.9
	12	104.4	102.6	1080	9.1	0.58	0.28	0.11	0.10	....	....	6.3	....
Period II.													
39 Cal. per kg. 6.8 gm. N. N. Bal. = — 10.3	13	105.0	102.4	1200	17.1	0.87	0.47	0.22	0.20	0.88	84.5	5.1	5.1
	14	104.2	103.0	1960	16.1	1.03	0.46	0.19	0.21	0.50	85.1	6.4	3.1
	15	104.3	102.0	1320	15.0	0.81	0.47	0.22	0.22	0.89	82.7	5.4	5.9
	16	104.4	103.0	1170	16.0	0.79	0.47	0.27	0.25	0.49	86.0	5.0	3.1
Period III.													
46 Cal. per kg. 4.4 gm. N. N. Bal. = — 5.4	17	104.2	102.0	1050	9.6	0.47	0.29	0.18	0.15	0.38	84.7	4.9	4.0
	18	104.8	102.6	....	....	....	....	....	....	....	....	....	....
	19	104.8	101.0	1500	9.6	0.49	0.31	0.16	0.16	0.63	81.9	5.1	6.5
	20	103.6	99.0	1340	8.3	0.49	0.26	0.12	0.13	0.46	82.3	6.0	5.5
Period IV.													
47 Cal. per kg. 9.8 gm. N. N. Bal. = — 4.6	21	103.4	99.0	700	8.8	0.34	0.31	0.10	0.16	0.55	83.7	3.8	6.2
	22	103.8	99.0	400	....	....	....	....	....	....	83.3	5.4	5.4
	23	101.8	99.0	620	13.0	0.54	0.36	0.18	0.13	0.59	87.3	4.2	4.5
	24	102.0	98.2	1000	12.7	0.59	0.36	0.19	0.13	1.03	83.0	4.7	8.1
Period V.													
40 Cal. per kg. 10.1 gm. N. N. Bal. = — 1.5	25	101.4	98.4	1080	10.8	0.52	0.34	0.15	0.11	0.92	81.2	4.9	8.5
	26	102.0	98.0	740	....	....	....	....	....	....	84.8	4.5	5.6
	27	101.4	98.4	950	9.4	0.40	0.30	0.14	0.08	0.57	84.2	4.3	6.0
	28	100.2	99.0	800	9.9	0.40	0.30	0.11	0.08	0.41	86.9	4.0	4.1

TABLE 31.—PATIENT 10, K—R: DAILY FOOD AND ANALYSES OF URINE.
Weight about 50 Kg.

Average Daily Food and Nitrogen Balance.	Day of Disease.	Temp. F. High.	Temp. F. Low.	Urine. Volume c.c.	Urine. Total N.	Urine. NH_3 N.	Urine. Kreatinin N.	Urine. Kreatin N.	Urine. Uric Acid N.	Urine. "Rest" N.	Per Cent. of Total N. Urea.	Per Cent. of Total N. NH_3.	Per Cent. of Total N. Rest.
					Period I.								
	13	104.0	102.0	1020	17.4	0.88	0.47	0.11	0.10	1.17	84.5	5.1	6.8
	14	103.4	101.4	....	....	....	....	....	....	....	....	....	....
97 gm. Fat	15	102.0	99.0	1060	15.2	1.14	0.44	0.02	0.13	1.35	79.8	7.5	8.9
468 gm. C. H.	16	103.0	99.0	420	....	....	....	....	....	....	....	....	....
8.5 gm. N.	17	102.4	99.4	840	12.0	1.06	0.46	0.10	0.13	0.98	77.3	8.8	8.2
60 Cal. per kg.	18	103.4	100.0	900	10.0	0.93	0.45	0.11	0.13	1.28	71.0	9.3	12.8
N. Bal. = — 6.4 per day..	19	102.4	99.0	1800	....	....	....	....	....	....	....	....	....
	20	100.0	99.0	....	....	....	....	....	....	....	76.1	7.3	11.7
Normal Temperature.					Period II.								
	1	99.4	98.4	1360	12.2	0.71	0.45	0.18	0.12	1.14	78.7	5.8	9.3
	2	99.4	98.4	....	....	....	....	....	....	....	....	....	....
118 gm. Fat	3	98.8	98.4	975	10.8	0.72	0.36	0.19	0.10	1.12	77.0	6.7	10.4
463 gm. C. H.	4	99.8	98.0	1350	9.4	0.57	0.33	0.17	0.05	0.97	77.9	6.1	10.4
9.3 gm. N.	5	100.0	98.0	1100	9.1	0.50	0.34	0.14	0.09	0.85	79.1	5.5	9.3
65 Cal. per kg.	6	100.4	98.0	1110	8.6	0.45	0.34	0.13	0.08	0.66	80.2	5.3	7.7
N. Bal. = — 1.9.	7	100.0	98.0	1110	8.6	0.45	0.34	0.13	0.08	0.66	80.2	5.3	7.7
	8	99.2	98.2	....	....	....	....	....	....	....	....	4.6	9.5
Relapse.					Period III.								
	1	101.4	99.0	1650	9.7	0.48	0.35	0.14	0.07	0.90	80.0	5.0	9.3
128 gm. Fat	2	103.4	100.0	1300	9.5	0.50	0.37	0.13	0.09	1.00	78.3	5.2	10.5
510 gm. C. H.	3	104.0	99.2	930	7.2	0.74	0.27	0.06	0.07	0.85	72.3	10.3	11.8
8.9 gm. N.	4	104.6	102.0	1125	10.2	0.46	0.43	....	0.10	0.83	82.3	4.5	8.2
70 Cal. per kg.	5	104.4	102.0	910	11.7	0.57	0.51	....	0.12	1.35	78.1	4.9	11.6
N. Bal. = — 2.0.	6	102.0	100.4	1480	8.0	0.62	0.37	0.00	0.08	1.34	69.9	7.8	16.8
	7	100.6	98.6	1220	10.5	0.81	0.40	0.00	0.12	....	....	7.7	....
Convalescence.					Period IV.								
	1	99.6	98.4	960	12.3	0.98	0.44	....	0.13	....	....	....	....
156 gm. Fat	2	99.0	98.4	1230	8.0	0.72	0.32	....	0.10	....	....	....	....
540 gm. C. H.	3	99.6	98.4	1390	7.3	....	0.32	....	....	....	....	....	....
13.2 gm. N.	4	99.0	98.4	1675	....	....	....	....	....	....	....	....	....
80 Cal. per kg.	5	100.0	97.9	1640	11.4	....	0.34	....	0.11	....	....	....	....
N. Bal. = + 1.4.	6	100.0	97.4	860	....	....	....	....	....	....	....	....	....

The difference in the nitrogen balance of these periods must be, in large part, due to the difference in intensity of the katabolic processes.

The Nitrogen Partition of the Urine in Typhoid Fever.

In addition to the data on this topic contained in the experiments already described, results from the analyses of the urine in three other severe cases are given in Tables 29, 30 and 31.

Patient 8—P—s, 31 years of age, admitted the tenth day of the disease. Positive blood-culture. Illness very severe. Duration of temperature sixty-seven days. Complicated by intestinal hemorrhage. Marked emaciation.

Patient 9—O—y, laborer, 21 years of age, poorly nourished, admitted the sixth day of the disease. Blood culture positive. Illness severe. Duration of fever twenty-eight days. Complicated by cholecystitis, without jaundice, and furunculosis. Emaciation during the illness marked.

Patient 10—E. K—r, lithographer, 15 years of age, admitted the eighth day of the disease. Positive blood culture. Illness moderately severe. Duration of fever twenty-one days, followed by a relapse. Complication, otitis media.

Kreatinin—From the work of Folin (34) and others (35) we know that in health the amount of this substance excreted is independent of the total amount of protein katabolized, and is practically constant from day to day, and from hour to hour. It has been further shown that the amount excreted by different individuals bears a definite relation to the weight (34), muscular development and strength (36) of those individuals. Kreatinin is essentially a product of endogenous metabolism (34), but is not a measure of the total endogenous metabolism (36). The truth of the latter statement is well shown by the kreatinin excretion by subjects of typhoid fever. With the increased katabolism of fever there is usually an increase in the amount of kreatinin excreted, as has already been shown by Leathes (37), but by no means in proportion to the total amount of the body protein katabolized. In considering the question of an increase or decrease of kreatinin excretion we must not base any conclusion on the absolute amount excreted, because of the great normal variations in different individuals; but must consider the relative amount per kg. of body weight. The highest relative excretion of kreatinin observed during these experiments is 10.6 mg. kreatinin-nitrogen per kg., the "kreatinin-coefficient" of U-h (Experiment 2, Period I, see Table 8), at which time the subject was losing about 9 gm. of nitrogen per day, and his total endogenous katabolism was therefore greatly increased. The normal kreatinin-coefficient of this subject, a laborer, was certainly not less than 9, which gives a probable increase of less than 20 per cent. in the kreatinin excretion at the height of the fever. The other experiments show in general the same rule: a marked, though relatively rather slight, increase during the height of the fever. This increase is very clearly shown by those patients who suffered a relapse (see Tables 15, 24 and 28). With, or even before the fall in the temperature, there is a progressive decline in the kreatinin excretion, this decrease apparently going somewhat parallel with the lowered muscular strength of the individual, although the kreatinin-coefficient does not usually fall so low as is often seen in subjects of chronic diseases (38).

The lowest relative kreatinin excretion observed in these subjects were about 4 and 5 mg. kreatinin-nitrogen per kg., found late in the disease with P——s (Table 29) and G——t (Table 28) respectively; and these were the patients who suffered the longest and most severe illnesses of the series.

In order to gather more accurate data from these patients regarding the relation between muscular strength and the amount of kreatinin excreted, a few measurements with a hand dynamometer were made on seven days early in convalescence on W——d, G——t, and B——t.

Five tests with two-minute intervals were made with each hand on each day. These tests were made after the end of the experiments and the kreatinin excretion at the time is not known, but the latter had probably not greatly changed from the values found in the last period of the respective experiments, and these values are therefore used in the accompanying comparison. The readings of the dynamometer are given in kilos.

While the tests with such an instrument are not very exact, and allow us to judge the strength of only one set of muscles, the results are fairly satisfactory and show very strikingly that the strongest subject excreted relatively the most kreatinin (39).

The increase of kreatinin excretion during the height of the fever, as has already been pointed out by one of us (40), is an exception in the relationship of kreatinin to

muscular development; but, aside from this exception, the amount of kreatinin excreted per kg. of body weight runs parallel with the "muscular efficiency" of the individual.

TABLE 32.—PATIENT 7, G—T: MEASUREMENTS WITH HAND DYNAMOMETER.*

Day of Convalescence						
27	29	31	32	33	34	35
			Right Hand.			
Kg.	Kg.	Kg.	Kg.	Kg.	Kg.	Kg.
18	21	20	22	20	22	25
19	18	20	20	22	23	22
18	20	21	20	21	21	20
18	20	18	20	21	23	23
18	20	21	22	22	23	23
			Left Hand.			
18	20	19	18	18	18	20
17	17	20	18	18	19	18
18	20	17	18	19	21	18
15	18	18	19	21	18	20
17	20	19	20	21	21	20
—	—	—	—	—	—	—
			Average.			
17.6	19.4	19.3	19.7	20.3	20.9	20.9
			Average of all Readings.			
..	..	..	19.7	..	..	..
			Kreatinin Coef.			
..	..	..	5.2	..	..	..

* Test began ten days after end of experiment.

TABLE 33.—PATIENT 4, W—D: MEASUREMENTS WITH HAND DYNAMOMETER.*

Day of Convalescence						
11	13	15	16	17	18	19
			Right Hand.			
Kg.	Kg.	Kg.	Kg.	Kg.	Kg.	Kg.
25	20	25	27	30	30	30
27	23	27	27	32	32	34
27	27	27	28	31	31	34
25	25	29	26	28	30	32
23	27	23	29	31	30	32
			Left Hand.			
23	15	23	21	28	27	28
23	17	21	24	29	28	27
24	16	24	25	27	27	26
22	21	25	21	28	24	25
18	18	23	25	23	24	25
—	—	—	—	—	—	—
			Average.			
23.7	20.9	24.7	25.3	28.7	28.3	29.3
			Average of all Readings.			
..	..	..	25.8	..	..	..
			Kreatinin Coef.			
..	..	..	7.0	..	..	..

* Tests began three days after end of experiment.

Kreatin—The behavior of this substance in typhoid fever has already been referred to. It is excreted in large amounts at the height of the disease if the subject is losing large quantities of body protein (see Table 29, the subject of which lost much body nitrogen throughout the greater part of the experiment). We believe that the kreatin excreted under such circumstances is directly derived from muscle tissues, and that its appearance in the urine indicates that muscle tissues are being destroyed.

TABLE 34.—PATIENT 5, B—T: MEASUREMENTS WITH HAND DYNAMOMETER.

Day of Convalescence				
11	13	15	16	17
		Right Hand		
(28)	39	41	35	41
37	37	36	40	43
36	40	40	43	44
41	35	39	39	44
37	33	40	42	40
		Left Hand.		
36	36	37	36	41
35	28	34	40	38
38	30	35	37	37
36	31	35	38	38
34	30	37	36	39
—	—	—	—	—
		Average.		
36.7	38.8	37.4	38.6	40.5
		Average of all Readings.		
..	..	37.4	..	..
		Kreatinin Coefficient*		
..	..	8.3	..	..

* Average of last ten days of Period V=0.615 gm. Kreatinin—N. Divided by 74 Kg.=8.3.

Uric Acid—Except for the few instances, the diets used contained no purins, and we are therefore concerned only with endogenous uric acid. Our results show as a rule a marked increase in the excretion of this substance during the height of the fever, followed usually by a decline with the fall of the temperature. The amount excreted varies with different individuals and each experiment should be considered by itself. With some of the subjects the uric acid remained high well into convalescence (Tables 28 and 29), while with others it fell in convalescence to probably below the normal (Tables 8, 29 and 30). The high uric acid excretion during the fever is in accord with the observations of Leathes (37) and others.

Xanthin Bases—A. R. Mandel (41 has determined the amount of xanthin bases excreted by three subjects of surgical fevers and by one subject of pneumonia, and finds a maximum of about 60 mg., calculated as xanthin, in twenty-four hours, as compared with the probable normal of about 20 or 30 mg. On the basis of these results, together with the fact that a rise in temperature follows the injection or ingestion of xanthin bases. Mandel apparently concludes that substances of this nature are primarily responsible for the febrile temperature. We can scarcely agree with this view. According to our results the excretion of xanthin bases bears no constant relation to the height of the temperature. With Z——o, for instance (Table 12), the xanthin increases with the slow fall in the temperature, the reverse of Mandel's finding. With B——t (Table 20) the same is true except that the highest amount (81 mg.) was excreted during the relapse. With L——d (Table 24) there is little difference between the periods of fever and of normal temperature. With W——d (Table 16) the highest amount, 91 mg. xanthin, is found at the height of the disease, but the lowest 30 mg., appears during a relapse when the temperature was moderately high.

Most of our results are abnormally high, according to Mandel's standard (42), but are not high when compared with the results of Camerer (43).

We find no evidence in our experiments that the xanthin bases are increased in typhoid fever or that the amount excreted bears any constant relation to the febrile temperature, thus failing to confirm either Erben (44) or Mandel.

Urea, Ammonia and "Rest" Nitrogen—Folin (46) has shown that for the judgment of the normality or abnormality in the excretion of these substances, or "fraction" in the case of the "rest nitrogen," it is necessary to consider the amount of total nitrogen excreted. Table 35 contains the normal limits, compiled from the results of Folin and of one of us, for the excretion of these substances. The figures are based on the analyses of about 200 urines, from a large number of normal persons. On the basis of these standards it is rather surprising that we do not find any very marked deviations from the normal in these subjects of typhoid fever. There are many instances in each experiment of increased excretion of ammonia and "rest" nitrogen, but the increase is rarely great, and not at all comparable to the figures obtained by Ewing and Wolf in the toxemias of pregnancy and allied conditions. On the whole our results justify the conclusion that during the height of the disease or during a relapse there is usually a slightly higher "rest" nitrogen and ammonia excretion than is found either normally or in the less active stages of the disease, but that the differences are usually not great enough to warrant the belief that the urea-forming process is necessarily seriously interfered with in uncomplicated typhoid fever.

The almost, if not quite, normal urea and "rest" percentages at times when the subjects were losing much body protein-nitrogen are especially instructive in showing that the protein of body tissue is at least under these conditions katabolized in the same way as food protein (46). (See Table 8, Periods I and III; Table 12, Period III; Table 20, Peroids I, II, etc.)

Table 35—Probable Normal Limits in the Excretion of Ammonia and "Rest" N.

	Per Cent. of Total Nitrogen.					
	Urea.		Ammonia.		"Rest."	
Gms. of Total Nitrogen.	Low.	High.	Low.	High.	Low.	High.
3 to 5.9.....	56	79	4	13	4	15
6 to 9.9.....	72	85	2	7	5	10
10 to 14.9.....	80	89	2	6	4	9
15 to 22	85	90	2	5	2	7

We should, of course, not conclude from our results that one never finds in typhoid fever very marked abnormalities in the excretion of urea and rest nitrogen. Ewing and Wolf (47) have found low urea and high "rest" nitrogen percentages in fatal cases. We have had no fatal cases in this series, though many of the subjects were severely ill. From the fact that most of our subjects did not show a very marked increase in "rest" nitrogen or decrease of urea percentage we are led to the conclusion that a serious interference with the urea-forming function is not an essential part of the process of typhoid fever, and that, when such marked abnormalities of this function appear in this disease, as found by Ewing and Wolf, they are the result of factors complicating the disease. And by such complicating factors we mean not the common accidents, like intestinal perforation, but rather a serious damage to the liver or other important organs, perhaps involving cellular degenerations, and thus interefering with the functions of these organs.

The ammonia excretion in these experiments was usually somewhat increased during the active stages of the disease, this increase being on the whole greater than the increase of "rest" nitrogen. The high ammonia is probably coincident with an increased excretion of organic acids; diacetic and oxybutyric acids were never found, even at those times when the subjects were not receiving much carbohydrate. The amount of ammonia was moreover never large enough to indicate any considerable acidosis. The ammonia excretion in these subjects does not appear to have been affected by the intake of carbohydrate, as it would be in the presence of an oxybutyric acid acidosis.

The Sulphur Partition of the Urine in Typhoid Fever.

Total Sulphur—Since the sulphur of the urine is derived chiefly from food or tissue protein the amount of total sulphur excreted usually bears a fairly constant

relation to the amount of total nitrogen of the urine. As might be expected this relation varied somewhat with different diets. With a milk-egg diet, with or without meat, between 7 and 8 parts of total sulphur are excreted for each 100 parts of total nitrogen (48). The same relationship was found in the urine of these subjects of typhoid fever, whether they were losing body protein or retaining food protein. The ratio between total sulphur and total nitrogen was with W——d (Table 16) 7.5 when he was losing 11.3 gm. of body-protein nitrogen per day and 7.3 when he was gaining 3.7 gm. nitrogen per day. Much the same thing is seen with Z——o and B——t (Tables 12 and 20). The ratios are in several instances below 7, but are, on the whole, remarkably constant.

The fact that an equivalent amount of sulphur is excreted with the nitrogen, even when the subject is losing body protein, is of interest in showing that the effect of carbohydrate in decreasing the nitrogen excretion in fever is not to be explained by a mere temporary retention of amino-acids of the food protein in the form of amino-sugars (Lüthje 49). Were this the case we should expect, on withdrawing the protecting carbohydrate, a sudden excretion of the retained nitrogen without an accompanying amount of sulphur (50). On withdrawing the carbohydrate from Z——o (Tables 11 and 12) in Period III the nitrogen excretion increased over 50 per cent., and the total sulphur increased practically in proportion. In Periods I and II, when there was great protection from the febrile loss of body nitrogen, the nitrogen sulphur ratios were normal, again indicating that the body protein was actually protected from taking part prominently in the febrile katabolism. Had the carbohydrate caused merely a retention of amino-acids this ratio might well be abnormally high.

Ethereal Sulphur—This fraction of the sulphur excretion by our subjects was within the normal limits, usually between 0.02 and 0.07 gm. This fact and the usual absence of a large excretion of indican gave no indication of excessive intestinal putrefaction.

Neutral Sulphur—This fraction of the sulphur partition was uniformly much increased above the accepted normal values of 0.10 to 0.15 gm (51). The highest amounts were excreted during the height of the fever, and fell to within normal limits with the decline of the temperature. The amount of neutral sulphur excreted in this disease bears no constant relation to the total sulphur, to total nitrogen, or to the loss of body-protein-nitrogen, and the significance of the febrile increase in this fraction is not at present clear.

Subjects of fever are supposed to be especially prone to alimentary glycosuria; and we rather expected to find a considerable excretion of sugar during the times when our patients were taking large quantities of lactose and other carbohydrates. Small quantities of sugar, rarely more than traces, were occasionally found in the urines during these experiments. The amounts were not large enough for accurate determination by titration with Fehling's or Pavy's solutions, and probably never exceeded 0.2 per cent., or a maximum of about 6 gm. in twenty-four hours.

Theoretic Considerations.

We have seen on a number of occasions in the preceding pages that, during the active stages of the disease, *a loss of body protein may be wholly prevented* by the intake of food of sufficient caloric value. These instances show very conclusively that the febrile destruction of body protein, including *both the effect of pyrexia and of toxins,* in the human subject of typhoid fever, may be either prevented altogether *or* may be compensated for by a large retention of body protein. As stated earlier in this paper, other experiments have indicated that the effect of pyrexia in causing an increased katabolism of protein may be prevented, but so far as we know the experiments here recorded are the first to show satisfactorily in the human subject that the action of toxins, as well as of the pyrexia, may be prevented from causing a loss of body protein by the addition to the food of a sufficient quantity of carbohydrate.

What is the probable explanation of this sparing of protein by carbohydrate in fever? Do we, by food of high caloric value, actually retard or prevent the febrile destruction of the body protein, or do we cause an increased retention of food protein which masks the destruction of body protein?

This very important question we, of course, do not hope to answer conclusively in this paper, but certain of our results have a very direct bearing on this consideration.

Results based wholly on the comparison of the intake and excretion of nitrogen, the nitrogen balance, show merely the final gain or loss of nitrogen to the body; they do not show variations in the extent of the endogenous metabolism; they do not tell us the amount of body protein destroyed in fever any more than they tell us the

amount of protein destroyed in the normal endogenous katabolism. The nitrogen balance in our experiments shows that the loss of protein in fever becomes less or may be prevented by food of high carbohydrate value. We might interpret this in at least two ways; that the large food-supply causes merely a retention of food protein or other nitrogenous substances, thus masking the destruction of body protein; or that the large food-supply has furnished all of the required energy and in available form to maintain equilibrium, and that the body found it no longer necessary to use its own material for that purpose.

Should we accept the idea of Krehl of an actual destruction of the protein of body cells by bacterial toxins we must also accept the first explanation of our result, because it is improbable that such a toxic destruction can be prevented by any form or amount of food. But Krehl's idea of the toxic destruction has by no means been proved to be correct, and there is one point brought out in our experiments and already referred to which we think distinctly favors the other interpretation—i. e., that the chief effect of the large carbohydrate intake is actually to protect the body protein from taking part in the excessive katabolism. This point is the behavior of the kreatin excretion. We have already considered this matter in some detail and need not repeat it here further than to say that endogenous kreatin, so far as we know, is excreted only when there is an abnormal absorption of muscle protein; that we have found it excreted in large amounts by the subjects of our experiments when they were at the same time losing much body protein; *and that it was not excreted,* or at any rate in but small amounts, *when the same subjects were being protected from the loss of body protein by food of high caloric value and rich in carbohydrates.* It therefore seems very probable that such food in some way greatly retards and, if sufficient, may even prevent the "toxic" or other destruction of muscle protein.

The relative constancy of the relationship between total nitrogen and total sulphur, which has already been referred to, is another indication of the same character.

Whether the above conclusion is wholly sound, further work will have to determine. It may well be that there remains a relatively small effect of toxins on the protein katabolism which may not be influenced by food, for, as we have seen, small amounts of kreatin were often excreted when the subjects received a very large supply of food and when they were even gaining nitrogen. Kreatinin, uric acid, and neutral sulphur are usually high during the active stages of the disease, whether or not the food value is high, and the endogenous katabolism concerned with these substances may be independent of the food supply. But we believe our results show that *quantitatively the most important part of the febrile destruction of body protein (in typhoid) may be retarded or prevented by food containing a moderate amount of protein and very rich in carbohydrate.*

The total caloric value of the diets used in the periods of great protection of body protein is very high, 60 to 90 cal. per kg. Whether such large amounts of food were actually utilized within the organism it is impossible to learn from our data. We have had no facilities for determining the total energy exchange, but, from the few such determinations which had been made on fever subjects, it is perhaps improbable that the total heat production of our patients reached the values represented by the larger amounts of food.

It seems to us more probable that the carbohydrate is the essential constituent of the food, and that the same sparing of body protein might have been accomplished had the fat been withdrawn from the various diets. The basis for this opinion is, however, not wholly satisfactory, for the data in our experiments regarding the relative value of fat in sparing body protein are not clear. This point awaits further investigation.

If fat does not assist in the protection of body protein from the febrile destruction the sparing observed during these experiments is to be referred to carbohydrate alone. The carbohydrate value of the diets used during the most favorable periods was between 40 and 50 carbohydrate calories per kg., and this amount, or even more, is necessary to prevent wholly a febrile loss of body protein. It may be that in carbohydrate alone we must supply more energy than equals the total heat production; and, if so, the situation is similar to that of the experiment by Murlin (52), who found that 125 per cent. of the maintenance requirement in the form of carbohydrate, when given to a dog, spared 49 per cent. of the starvation excretion of nitrogen, while 100 per cent. of the requirement spared only 23 per cent. of the starvation excretion.

The typhoid subject who is losing body protein (62.5 gm.) equivalent to 10 gm. of nitrogen per day derives from this protein only 250 cal., and it seems very remarkable that, to prevent this loss, we must given him additional carbohydrate equivalent to 2,000 cal. or more. The same is true in simple starvation. In neither instance have we at present any explanation of this apparent anomaly. In both cases it is

evident that the use of the carbohydrate is not a mere replacement of isodynamic quantities of protein. Some insight into these questions will doubtless follow investigations of the total energy exchange in fever subjects receiving diets containing varying quantities of carbohydrate. At the present time an adequate explanation of this action of carbohydrate is not possible.

Practical Therapeutic Considerations.

We have so far avoided any discussion of the therapeutic value in typhoid or other acute infectious fevers of the protection from the katabolism of body protein afforded by diets rich in carbohydrates, for the reason that we have not accumulated sufficient data to judge this question. It seems to us obvious that unless there are distinct and forceful objections to such dietetic treatment the subject of the disease will be better off if he is not permitted to use up his body material. Unless we gratuitously assume the febrile destruction and loss of body protein to be a beneficial process, it is difficult to avoid the conclusion that we are ministering to the welfare of the patient by preventing that destruction or loss. We have so far encountered clinically no valid objection to the use of such diets as those of the experiments here described, and, unless future experience proves such objection, we believe it highly desirable to retard and, if possible, prevent the febrile loss of body protein.

The general nutrition of the subjects of our experiments was exceptionally good at the end of the disease, many weighing more at the time of discharge than when they entered the hospital.

A more detailed discussion of the strictly clinical aspects of this question will be attempted in a future paper.

Conclusions.

As a result of our experiments the following conclusions may be drawn regarding the protein metabolism in typhoid fever:

1. By the use of diets of high caloric value and especially rich in carbohydrate it is possible to retard and, if the carbohydrate supply be sufficient, to prevent the febrile *loss* of body-protein-nitrogen in subjects of typhoid fever.

2. By such dietetic treatment the "toxic" destruction of body protein as well as the destruction due to simple pyrexia in this disease may therefore be *either prevented or compensated for.*

3. The behavior of kreatin and of total sulphur in our experiments appears to show that the febrile destruction of body protein, including the action of pyrexia and of toxins, is actually retarded or even wholly prevented by the intake of sufficient carbohydrate.

The prevention of the febrile loss of body protein is therefore probably not to be explained by a mere compensatory retention of food protein.

4. The results support the belief that in fever there is a greater need for carbohydrate; that if the food does not contain sufficient carbohydrate the body protein is drawn on perhaps to supply energy in an available form; but that, if sufficient carbohydrate be available from the food, the body protein is protected from the febrile destruction.

5. If, as seems probable from our results, the "toxic" destruction of body protein may be prevented by large carbohydrate intake, the mechanism of this "toxic" destruction cannot be a direct (poisonous) injury to body cells and proteins.

6. To maintain nitrogen equilibrium in typhoid fever the food must contain 10 to 15 gm. nitrogen in addition to much carbohydrate. Our experiments show no advantage from a further increase of food-protein.

We take pleasure in expressing our obligations to Dr. Armstrong, to Miss Goodrich, to Drs. W. M. Kerr, T. S. Kearns, members of the resident staff of the second division of Bellevue Hospital, for many courtesies and assistance during the work; to Mr. M. I. Smith and Dr. G. H. Bentz for assistance in the laboratory, and to Dr. C. L. Dana for the privilege of continuing the work during his service in the hospital.

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22. A similar blank had been previously used by Folin and one of us (Shaffer) at the McLean Hospital. Printed blanks also were used daily for recording in the ward the amount and kind of food taken by each patient. To the advantages derived from the use of these blanks we attribute in large measure the technical success of our experiments.
23. The feces of Hoesslin's typhoid subjects (Virchow's Arch. f. path. Anat., 1882, lxxxix, 317) contained on the average about 1 gm. nitrogen per day. Leyden and Klemperer's subjects excreted usually between 1 and 2 gm. nitrogen in the feces, the amount increasing with the nitrogen of the food. In one case the last-named worker assumed the feces-nitrogen to be 10 per cent. of the food nitrogen. In our own analyses, the feces-nitrogen amounts to between 10 and 20 per cent. of the food-nitrogen.
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PROTEIN METABOLISM IN PNEUMONIA.*

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It might be assumed in a disease of such common ocurrence and such fundamental importance in medicine as pneumonia that a very complete account of the protein metabolism would be available, especially in view of the fact that the conditions of the disease are such as to put at the disposal of the observer a sudden change in the condition of the patient from a condition of high temperature, great dyspnea and

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rapid heart action, to a normal state, which scarcely has a parallel among other diseases. Incident to this, one has also a rapid change in the anatomical condition of a vital organ, the lung, in which, as Müller, and his pupil, Simon (1), showed large quantities of soluble and partially digested protein products are thrown into the circulation and catabolized.

Observations of Early Investigators—In examining the literature bearing on the metabolism of the disease, one is struck with the relatively small amount of accurate information. In some instances determinations of the daily output of nitrogen have been made, many without reference to the nitrogen of the food. In most other instances investigators have contented themselves with an examination of a single component of the urine, such as uric acid, chlorids, xanthin bases, etc. As a matter of fact, the work which was done forty years ago by Huppert and Riesell (2) is more instructive and gives a clearer picture of the effect of the infective process on the elimination of nitrogen than any of the late investigations. Even before their time also there were observations which showed the excessive amount of nitrogen eliminated.

Total Nitrogen.

Parkes, in his excellent book on "The Composition of the Urine" (London, 1860), gives the amount of urea found by a number of observers, and adds the report of a case examined by himself in which 85.38 gm. of urea were eliminated in a single day. This amount of urea would be equivalent to 40.7 gm. of nitrogen. As Parkes states that the patient was in a condition of fasting, this amount of nitrogen would be equal to 1,200 gm. of muscle or other tissue of a similar composition furnished by the body to carry on the metabolism during the period of hyperpyrexia. That the infective process was greatly concerned in this elimination of nitrogen will readily be seen when it is noted that 40 gm. of nitrogen is probably three times as much as a fasting subject would excrete under normal conditions of health.

Huppert and Riesell's observations were carried on with the elder Voit's investigations in mind. Not only was the nitrogen of the urine estimated, but also the nitrogen contained in the food, the sputum and the feces. In this way an accurate balance could be struck. The amount of nitrogen in the food during the period of hyperpyrexia and the resorption of the exudate was inconsiderable. The minus balance from day to day varied from 15 to 25 gm., the highest negative value being found on the day of beginning resorption. The following days, in which the patient took 4 gm. of nitrogen, there was still a marked daily deficit. It was only on the sixth day after resorption had begun that the loss in nitrogen suddenly decreased, coincidentally, however, with the administration of food containing 16.7 gm. of nitrogen. A retention of nitrogen was arrived at on the twelfth day with 25 gm. of nitrogen intake. Huppert and Riesell conclude that in conditions such as pneumonia the patient burns the cellular protein in contradistinction to the nutritive protein, which the healthy individual uses for catabolism. In this they approach very closely the idea of toxic destruction of protein so much debated by late writers.

In recent years the work of Moraczewski (3) on the metabolism in pneumonia appears to be more complete than that of any other observer. His studies of the protein metabolism in fever were directed to show that the tissues imbibed water during the course of hyperpyrexia and that this imbibition of water determined the increased protein decomposition. He attempted to ascertain if by "salting out" the blood it might be possible to inhibit increased destruction of protein. Moraczewski was one of the first to make an attempt to fractionate the components of the nitrogen elimination. Unfortunately, a close examination of the analytical results which this investigator furnishes does not lead one to place great weight on his work. His theoretical conclusions and his methods of experimentation (the administration of silver nitrate to reduce chlorid content of the blood) have been subject to what appears to be just criticism by Magnus-Levy.

Von Jaksch (4) has also made a comparative study of pneumonia and typhoid fever. He finds a notable difference in the manner in which the nitrogen compounds of the urine are eliminated in the two diseases.

According to this observer, pneumonia is classed with those diseases in which the nitrogen partition is normal, none of the nitrogen which is normally excreted as urea being used for the formation of other compounds. On the other hand, the catabolism in typhoid fever, according to von Jaksch, takes a distinctly abnormal course and instead of urea being eliminated in its normal ratio to total nitrogen the substance is replaced by other compounds—leucin, tyrosin and unknown substances. Unfortunately here also the methods employed for the analyses have been open to criticism, and von Jaksch has subsequently been forced to retract many of the statements which he previously made regarding the metabolism in these condi-

tions. To what extent von Jaksch's statements regarding typhoid are corroborated may be seen from the work which has been done by Ewing and one of us (5) in a recent paper.

Total Sulphur.

The total sulphur is taken up at this place before the distribution of the nitrogen is discussed, for the reason that the total sulphur in conjunction with the total nitrogen might give data regarding the type of protein metabolized at different stages of the disease.

As sulphur occurs in all protein with few exceptions, and as the sulphur content varies between 0.3 and 2.2 per cent., and the nitrogen content of protein varies between 15 and 17 per cent., there is a margin in the relation of sulphur to 100 parts of nitrogen of 1.7 to 14.6 per cent.

The relation of sulphur to nitrogen in normal urine is, however, a comparatively fixed value, being in the neighborhood of 7 per cent. With the ingestion of protein of varying sulphur content the organism apparently adapts the catabolism of the two compounds in such a way that the two are excreted in a fairly fixed ratio. It might be permissible to assume, however, in pathlogical conditions, especially those associated with the breaking down of large quantities of body protein, that the ratio of nitrogen to sulphur in the urine might be disturbed, and so one might obtain information regarding the catabolism of some special type of protein.

In experiments which one of us has made, it would appear that those compounds containing a relatively high amount of sulphur are of more importance to the organism than those containing less. Consequently, one might expect that during a time of toxemia when the factors of control were removed a high ratio of sulphur to nitrogen would obtain, while in the stage of convalescence this would be compensated for by a low sulphur-nitrogen ratio. To what extent this is the case will be seen throughout the discussion of the tables.

In some conditions of experimental toxemia, notably in delayed chloroform poisoning, the ratio certainly increases, Howland and Richards (6).

The Nitrogen Partition.

Ammonia—With regard to one constituent of the urine accurate information is very much to be desired. This is ammonia. In view of the important rôle which this product of intermediary metabolism plays in modern theories of acidosis and protein breakdown, it is remarkable that no particular attention has been paid to it in connection with a disease in which the excessive destruction of protein is so well recognized.

Hallervorden (7), in an examination of the ammonia output in pathological conditions, interpolates the reports of two cases of pneumonia, in one of which, however, the ammonia excretion was examined for two days only. In this case the ammonia excretion was lower on the day of higher fever. In the second case (Fiss) the ammonia rose during the first part of the lysis, and thereafter followed fairly closely the trend of the temperature curve. Hallervorden believes that the increased elimination observed in fever is associated with a retention of fixed bases—potassium and sodium—and that the ammonia is used by the organism in an attempt to protect itself from the loss of these substances. In accordance with the time at which Hallervorden performed his experiments, the Schlösing method was used for the estimation of ammonia. From the accounts he gives, it is quite clear that he had great difficulty in assuring himself of the accuracy of the method. In the course of the present investigations we have had to discard repeatedly specimens of urine on account of commencing decomposition, so that in the work of Hallervorden, and, indeed, through all the work in which the Schlösing method has been used, it is quite possible that variations are due to decomposition occurring during the estimation.

Uric Acid—The intimate relation between the leucocytes and the process of resolution has drawn attention to the purin compounds.

With regard to uric acid, Voges (8) and Friedrichsen (8), working in von Noorden's clinic, obtained normal values for uric acid. Dunin and Nowacek (9), in an attempt to connect Horbaczewski's theory regarding the connection of the leucocytes with the xanthin base excretion, found an increase in uric acid after the crisis, and this increase, they believe, was due to the breaking down of nuclein compounds during resolution. The increase persisted for two to four days, and was followed by a similar period of lessened output. Only on the seventh day after the crisis did the uric-acid excretion arrive at what they considered a normal value.

Simon (1), in his interesting study of the autolysis of pneumonia lungs, made under Müller's direction, found free alloxuric bases in the autolysate. One of the most recent investigations in this field is that of Carlyle Pope (10), who has compared the leucocytosis occurring in various conditions with the elimination of uric

acid and xanthin compounds. One case of typhoid and five of pneumonia were studied. In the hypoleucocytosis of typhoid he finds average amounts of uric acid and somewhat greater amounts of xanthin bases. In all cases of pneumonia there was, at certain times, an increase in the xanthin base elimination. There was not a true parallel between the hyperleucocytosis and the increased elimination of xanthin compounds. The increase took place after the disappearance of the hyperleucocytosis and simultaneously with the resolution of the pneumonic exudate.

Creatinin—Our information regarding the influence of pathological conditions on the output of creatinin is very scanty. Since the advent of the Folin method, most investigators have very properly confined themselves to the effect of physiological changes on the excretion of the substance. A few, Shaffer (11), Leathes (12), and Spriggs (13), have investigated some of the more important diseases, more especially those connected with disturbances of muscle function.

In high temperatures, Leathes found that the hyperpyrexia produced in a normal subject by the use of antityphoid vaccine caused a rise in the excretion of creatinin. In cases associated with loss of muscular tonus the excretion of creatinin is low relatively to the body weight. In Shaffer's results there is a record of a convalescing typhoid patient in whom the creatinin output was distinctly low. This will be found to agree with the condition in convalescence from pneumonia. After a period of excessive creatinin excretion the values suddenly fell to what must be considered decidedly subnormal. Case 20 of Shaffer's series shows that the creatinin co-efficient is very high (10) on the twelfth day of the disease, and falls on the forty-third day to 7.7. A more striking fall in convalescence is presented by Case 12.

Our own results confirm these findings, except that the transition is much more abrupt (see Case 12, H. C.).

Creatin—The information regarding creatin is much less complete than that of creatinin. We know but few facts which shed light on its pathological significance. Of these the first is its absence from normal urines of subjects on creatin-free diets, and second, its appearance in the urine of animals exposed to starvation or under-nutrition. It is also found in acute fevers (Ewing and Wolf), in exophthalmic goiter (Shaffer) and in women during post-partum resolution of the uterus (Shaffer).

The significance of these findings is obscure, but one may safely say that at the present time its appearance in the urine denotes either a condition of partial starvation or a pathlogical state.

Rest Nitrogen—The question of rest nitrogen is perhaps more complex than any of the previous components, by reason of the number of substances which enter into its composition. In the rest nitrogen in pneumonia are included two classes of compounds which have been closely associated with the disease. One of these is the xanthin bases which could not be determined separately except in a few cases, and whose amount is supposed to be decidedly increased in fevers (14).

The other group of compounds consist of the albumoses, or, as they are more frequently called in this connection, the peptones. Maixner (15) found them in pneumonia, mostly during the stage of resolution. Maixner says that he has seen 4 gm. of these substances in the twenty-four-hour amount of urine. In some of our cases the extreme amounts of undetermined nitrogen led us to examine for albumoses by the method of Devoto.

The composition of the undetermined nitrogen has been discussed by one of us with Ewing (16) in some detail in papers on the clinical significance of the urinary nitrogen, and it is unnecessary to repeat the points of the discussion here, except to point out that in normal subjects the amount of rest nitrogen does not increase in direct proportion to the total nitrogen, so that when one finds an increase one is led to suspect a faulty condition of metabolism, in that the steps leading to the ultimate formation of urea are not properly followed. This aberrance has been called defective desamidation. It will be noted that von Jaksch had this idea in mind when he differentiated typhoid fever from pneumonia, regarding the former as a disease in which defective splitting off of ammonia from the protein group played an especial part. In pneumonia this did not occur.

As will be seen, however, amounts of rest nitrogen are obtained in pneumonia which are unequalled in typhoid fever, so that the statement of von Jaksch does not altogether hold. It is true, however, that higher relative values for rest nitrogen are found in typhoid than in pneumonia, but only in daily excretions of nitrogen which are low when compared with pneumonia.

The Sulphur Partition—The reason for an almost complete lack of accurate data regarding sulphur excretions in pathological conditions arises from the difficulty of the analyses for the clinical investigator. While it is unlikely that the examination of the sulphur partition will give information regarding the oxidative capacity of the organisms as a whole, a study of the sulphates, alkaline and ethereal, will throw light

on the processes, putrefactive or otherwise, leading to the formation of ethereal sulphates and at the same time give us some knowledge of the obscure class of compounds making up the neutral sulphur.

As the neutral sulphur compounds must of necessity be included in the rest nitrogen, some conclusions may be drawn regarding the latter as to its content in sulphur-containing substances.

Nitrogen Loss—Before we take up the investigation of the individual components of the urine in a disease like pneumonia it is necessary to inquire what the effect of the individual factors entering into the condition is on the nitrogen metabolism as a whole.

The most obvious of these are high temperature, dyspnea, and infection, and, as a special factor in pneumonia, the resolution of the pneumonic exudate.

With regard to high temperature, most of the estimations of the nitrogen excretion in connection with hyperthermia have been made on cases under the influence of infection, and from these it is difficult to ascertain whether the increase is due to the rise in temperature by itself, or whether the so-called toxic destruction of protein is to be held accountable. Reasoning from purely chemical grounds, it would appear improbable that with a rise of temperature increased nitrogenous decomposition should not take place. We know that the velocity of chemical reactions increases with increments of temperature, and it would be necessary, if the opposite should be found to be the case in pathological conditions, to assume a physiological inhibitory factor interposed, of which, at the present time, there is no evidence. The one experiment in man bearing on the relation of temperature to nitrogen output is that of Linser and Schmid (17), who experimented with a patient suffering from ichthyosis hystrix. They showed that, on raising the body temperature to 39 C. (102.1-102.8 F.), which they were able to do by enclosing the patient in a room artificially heated, no increase in nitrogen output took place. If, however, the temperature of the room were further raised so that the body temperature reached 40 (104 F.) a decided increase in protein metabolism did take place. From this they inferred, and probably rightly, that they had demonstrated the effect of temperature alone in increasing the nitrogen metabolism. An examination of the increase which Linser and Schmid obtained shows that it is incomparably lower than what is obtained in infectious fevers.

In animals Voit (18) has shown that if the surrounding temperature of fasting animals be raised the nitrogen output is increased. On the other hand, if the animals be protected by the sufficient administration of carbohydrates and fat no comparable increase in the nitrogen metabolism takes place. It is probable that calorimetric investigation of these animals in superheated calorimetric chambers would disclose an increased metabolism, falling in this instance, however, on the carbohydrate and fat rather than on the protein, as in the starving animals. As the patients whom we examined were in most cases protected by an amount of food sufficient to give almost nitrogen equilibrium in a normal person, the excess output may be set down to factors other than simple hyperthermia alone.

The next factor in the increased nitrogen elimination in these cases is the dyspnea. In this field the investigations of Voit take the first place. In most instances Voit's experiments were carried out on animals in which dyspnea was produced by the mechanical occlusion of the trachea. The results were uniform in showing an increased elimination of nitrogen through the urine as a consequence of hindrance to the gaseous exchange. Voit, however, believes that the increased nitrogen excretion is not primarily due to lack of oxygen, but has its origin in the increased muscular effort of the animal.

Von Noorden (19) reports a case of syphilitic stenosis of the larynx. The amount of nitrogen excreted during the period of fasting was quite within the normal limits.

There remains to be considered the effect of infection on the excretion of nitrogen, and in this field much work has been done both on man and on animals.

It is practically impossible to separate the factors of infections from fever, and therefore the investigators who have worked on the effects of infection have always considered them together. While it is impossible to produce in animals a fever of the long-continued type seen in man, the experiments which have been made in animals are instructive in showing to what extent the protein metabolism may be raised by the combined processes of fever and infection.

May (20) was able to increase the nitrogen elimination in fasting rabbits 51.9 per cent. above the normal by infecting these animals with hog-cholera. Stähelin (21) infected dogs with surra and produced a very marked negative nitrogen balance. In dogs in nitrogenous equilibrium, on about 5.5 gm. of nitrogen, the deficit was 2.5 gm. in a single day, all of which was excreted in the urine. This, it will be seen, is very close to May's 50 per cent. increase in rabbits after hog-cholera infection. The knowledge of the effect of fever and infection in man on the excretion of nitrogen

is not complete, for it is impossible to determine accurately the state of nutrition of the individual before the infection process began, and one is forced to use as a standard for comparison either results obtained in normal individuals or the metabolism of the same patient during the period of convalescence. That these are not altogether trustworthy was recognized by Huppert many years ago.

A few experiments have been recorded by Leathes (12) on the nitrogen excretion in aseptic fevers produced by the injection of typhoid vaccine. The fever was neither continuous or excessive; nevertheless a distinct rise in the nitrogen metabolism was observed. Leathes' experiments have been confirmed by Kraus. As Kraus remarks (22), it is necessary to be extremely careful in any estimate of the nitrogen output in these cases, especially when they are connected with fasting, for the excretions on the third day of a normal fasting subject may vary from 8 to 15 gm.

The problem therefore in the following discussion of the total nitrogen excretion in pneumonia is to ascertain whether the nitrogen eliminated is to be accounted for by the dyspnea and the high temperature, or whether the amount excreted in the twenty-four hours exceeds what may be set down to the two non-infective factors.

If one adds to the high starvation value, viz., 15 gm., that which has been set down to rise in temperature, one still finds in these cases a very considerable amount of nitrogen which must be set down to the infection process alone. It will be observed that in practically all these cases (the exceptions are noted at the proper place) the patients were receiving amounts of nitrogen and units of heat almost sufficient to keep a normal individual in a condition of nitrogen equilibrium.

Experimental—The analytical methods employed in this work were those which have been employed by one of us through a series of investigations in normal and pathological metabolism. They were: total nitrogen, Kjeldahl; ammonia, Folin; urea, Folin; uric acid, Folin-Shaffer; creatinin and creatin, Folin; total sulphur, Folin; total and alkaline sulphates, Folin; chlorids, Volhard; phosphoric acid, uranium acetate.

The urines were preserved with chloroform-thymol-toluol, and were analyzed for ammonia and creatinin as soon as possible after collection. In some instances decomposition had apparently set in during the time they were collected. When this is suspected, it is noted in the tables.

In dividing the cases examined, we have decided to separate arbitrarily the fatal cases from those which terminated in recovery. In some respects a classification of this sort may appear unsatisfactory, but it has the advantage that one is able to correlate the results obtained by a chemical study with the factors which led to a fatal termination. Moreover, in the non-fatal cases we are able to follow the patient through his recovery, and from an examination of his metabolism to attempt to make this a part of the basis for clinical prognosis.

In all, 19 cases of pneumonia were examined during longer or shorter periods. Only 14 are reported on; the others do not throw any further light on the condition.

Our original intention was to study the effect of diets containing little or no protein, but a fairly large supply of heat in the form of carbohydrate and fat, and to compare this diet with one containing an amount of protein representing about 16 gm. of nitrogen. Our reason for doing this was based on a consideration of Benedict and Suranyi's (23) results, in which it was asserted that it was useless to administer large quantities of protein during the nitrogen loss in fever, as the increase in catabolism took place *pari passu* with the nitrogen intake.

Two cases are reported on this non-nitrogenous diet, but it was abandoned on account of the difficulty in inducing the patients to take it. Finally a standard diet was designed with a fair amount of protein, but which was unfortunately not very high in heat units.

It was as follows:

	Amount.	Nitrogen.	Fat.	Carbohydrate.	Calories.
Milk	1,080	5.6	43.0	54.0	765
Crackers	40	0.7	3.6	29 2	158
Boiled rice	120	0.3	0.1	29.0	135
Toast	60	1.1	9.6	36.0	156
Cream	60	...	13.5	2.4	145
Sugar	90	...	....	90.0	360
Total	..	7.7	69.8	240.6	1,719

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.*	Albumin.	Ethereal Sulphate Sulphur.	Per Cent. S.	Neutral Sulphur.	Per Cent. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
					Gm.		Gm.			Gm.	Gm.		
7	1005	1021	†	+ + +	0.08	5.7	0.21	15.0	13.2	0.43	0.06	96–80	103.6–101.4
8	1225	1021	†	+	0.04	2.3	0.25	14.1	46.3	0.43	0.22	100–72	100.0– 98.4
9	1025	1021	†	0	0.06	5.7	0.12	11.3	8.9	1.29	0.25	88–72	98.6– 98.0
10	No urine received.												
11	1605	1023	†	+	0.07	3.3	0.15	7.2	7.8	1.75	0.77	72–60	99.4– 99.0
12	960	1021	†	+	0.05	5.7	0.11	12.5	9.0	1.01	1.91	66–60	99.8– 98.6
13	1205	1010	†	0	0.03	8.3	0.09	25.0	26.4	0.38	1.66	76–60	99.0– 98.0

* In this and the following t

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.*	Albumin.	Indican.	Total Nitrogen.	Albumin Nitrogen.	Amid Nitrogen.	Per Cent. Total N.	Ammonia Nitrogen.	Per Cent. Total N.	Urea Nitrogen.	Per Cent. Total N.	Creatinin Nitrogen.	Per Cent. Total N.	Creatin Nitrogen.	Per Cent. Total N.	Uric Acid Nitrogen.	Per Cent. Total N.	Rest Nitrogen.	Per Cent. Total N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. S.	Alkali Sulphate Sulphur.	Per Cent. S.	Ethereal Sulphate Sulphur.	Per Cent. S.	Neutral Sulphur.	Per Cent. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. * Fahr.
						Gm.	Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			Gm.	Gm.		
7	1005	1021	†	+ + +	+ + + +	8.84	1.72	14.52	85.2	1.15	6.7	13.42	78.5	0.64	3.7	0.00	0.0	0.38	2.2	1.33	8.9	1.40	7.4	1.19	85.0	1.11	79.3	0.08	5.7	0.21	15.0	13.2	0.43	0.06	96–80	103.6–101.4
8	1225	1021	†	+	+	25.50	....	23.88	93.7	1.22	4.7	22.66	89.0	0.62	2.4	0.00	0.0	0.46	1.8	0.54	2.1	1.77	7.0	1.52	85.9	1.48	83.6	0.04	2.3	0.25	14.1	46.3	0.42	0.22	100–72	100.0– 98.4
9	1025	1021		0	+	20.17	....	18.09	89.7	1.02	5.1	17.07	84.6	0.49	2.5	0.00	0.0	0.24	1.2	1.35	6.6	1.06	5.3	0.94	88.7	0.88	83.0	0.06	5.7	0.12	11.3	8.9	1.29	0.25	88–72	98.6– 98.0
10	No urine received.																																		
11	1605	1023	†	+	+ + + +	30.18	....	26.93	89.2	0.96	3.2	25.97	86.0	0.77	2.5	0.00	0.0	0.55	1.8	1.93	6.5	2.09	6.9	1.94	92.8	1.87	89.5	0.07	3.3	0.15	7.2	7.8	1.75	0.77	72–60	99.4– 99.0
12	950	1021	†	+	+ + + +	13.45	....	13.50	87.4	0.36	2.3	13.14	85.1	0.37	2.5	0.13	0.8	0.23	1.5	1.22	7.8	0.88	5.7	0.77	87.5	0.72	81.8	0.05	5.7	0.11	12.5	9.0	1.01	1.91	66–60	99.8– 98.6
13	1205	1010	†	0	+ + +	7.06	....	6.46	91.5	0.25	3.5	6.21	88.0	0.19	2.7	0.00	0.0	0.07	1.0	0.34	4.8	0.36	5.1	0.27	75.0	0.24	66.7	0.03	8.3	0.09	25.0	26.4	0.38	1.66	76–60	99.0– 98.0

* In this and the following tables, an acid reaction is indicated by a dagger (†), and an alkaline reaction by a double dagger (‡).

It would have been advantageous to have increased the nitrogen about 5 gm. and to have given a great deal more carbohydrate and fat. At the time the work was done by Shaffer he had not obtained his very important results on diet in fever, and therefore we are obliged to present these cases with, in some instances, a nitrogen loss which we feel could have been partly avoided with a proper diet.

In some instances eggs were given during convalescence in accordance with the theories of Suranyi and Benedict (23). This is stated in the notes to the tables.

In taking up the individual cases, we shall discuss the findings in the first case in considerable detail, with the intention of using this case as a standard for future comparison. The others will to some extent be referred to the first one in pointing out the differences which occur. In this way a repetition of the findings will be avoided.

Mild Cases.

Case I—The patient, Z., male, 34 years of age, alcoholic, had a small area of pneumonia in right upper lobe. He was admitted on the eighth day of the disease, with mild attack; general condition excellent. He was slightly irrational on the night of admission. On the 19th his general condition still excellent, though he began to be delirious. Defervescence began and was completed on morning of 20th. During the 20th, 21st and 22d the patient had an abortive attack of delirium tremens, but his general condition and his pulmonary lesion improved steadily. On the 23d he was comfortable and rational, and from then on to the 29th there was uninterrupted convalesence.

The patient received the higher nitrogen diet, containing 12.1 gm. of nitrogen and 1,971 calories. The urine was first examined on the day of the crisis—the seventh day of the disease. On the eighth day the temperature fell to normal. The highest temperature recorded was 104.4, on the day before the examination commenced. The leucocyte count on the seventh day was 14,000.

Total Nitrogen—On the seventh day the total nitrogen excreted was 25.5 gm., and on the eleventh day of the disease, on which a slight post-critical rise occurred, the total nitrogen excretion rose to 30 gm. On the following two days the excretion was each day half that of the day preceding, giving for the last day of the examination 7.1 gm. It is to be noted that with the very high excretion of the eleventh day the patient was physically comfortable, and was well into an uneventful convalescence.

Amid Nitrogen—The percentage of total nitrogen excreted as urea and ammonia is low on the first day of the examination, but rises with defervescence. The highest ratio is obtained during the days of marked fall in temperature. This case would illustrate admirably von Jaksch's statement that pneumonia is a disease in which the catabolism of nitrogen proceeds in the same way as in the normal subject. The ratios of urea and nitrogen are almost as high as one observes in normal subjects. That this, however, is not so with the more toxic cases will be shown later.

Ammonia Nitrogen—A careful examination, not only of this case but of those which follow, leads one to believe that a comparative acidosis occurs. Taking normal individuals with an excretion of 15 gm. of nitrogen, the average amount of ammonia nitrogen excreted is about 0.5 gm., and the ratio of ammonia nitrogen to total nitrogen is 3.3 per cent. As will be seen, the amount of ammonia excreted during periods of pyrexia in pneumonia is distinctly higher than this, over 1 gm. of ammonia nitrogen being excreted. The ratio is also high—6.7-4.7 per cent. of total nitrogen. Both absolutely and relatively the ammonia nitrogen decreases during convalescence.

Urea Nitrogen—Compared with what one observes in typhoid fever, the ratio of urea nitrogen to total nitrogen is high. Compared with normal subjects, it is low. The difference in favor of normal urines is small, averaging perhaps 3 to 4 per cent.

Creatinin—Owing to the large amount of attention which has lately been directed to the output of creatinin in physiological conditions, contributions from the pathological side are at present of considerable interest. It is scarcely worth while at this point to review the literature on this subject, except to say it has been found that the daily output of creatinin is practically constant with great changes of diet. It is therefore assumed that the creatinin output represents a type of metabolism uninfluenced by the protein intake. It has also been found that in patients suffering from certain diseases associated with general loss of muscular tone the ratio of the creatinin excreted to the body weight is decreased, while, conversely, in those conditions in which it is supposed that the metabolism is proceeding at a higher level than normal creatinin coefficient is increased. In starvation, both in men and in animals, it is known that the creatinin output is lower, corresponding with the attempt of the organism to adapt its metabolism to the lessened food intake.

In a condition of very great metabolic activity, such as the hyperpyrexia of pneumonia, with the loss of 20 or more grams of protein nitrogen on a diet capable of maintaining a normal individual in a state of nitrogen equilibrium, it might be expected that during this period the endogenous metabolism would be increased, perhaps not *pari passu* with the total increase, but at least sufficiently to make its influence felt on the creatinin output. One would then have the ratio of creatinin nitrogen to total nitrogen decreasing with the rise in total nitrogen output, but the absolute amount of creatinin excreted would be increased. In the majority of cases this happens. During this hyperpyrexia the creatinin output is high as compared with normal individuals. In some instances the highest output is recorded during the stage of resolution. It would appear that at this time not all the creatinin is derived from endogenous metabolic processes. In pneumonia one has an autolytic process occurring in the lung which may apparently give rise to the excretion of increased amounts of creatinin through the urine. During convalescence the creatinin output is markedly decreased. Not only is the amount diminished, but a comparison with the normal amount excreted will show that it is from one-half to one-third lower than that which is considered normal for a person of average weight. Unfortunately, throughout this entire series it was impossible to take the weights of these patients, so that the creatinin coefficient (the ratio of creatinin to body weight) cannot be given. It is however, certain that in comparison with the results yielded by normal subjects the creatinin is much higher during hyperpyrexia and falls during convalescence to very low values.

It can scarcely be doubted that after a period of great prodigality of its resources, such as occurs in severe toxic conditions associated with high temperature, the organism seeks to conserve its remaining store of energy to the limit of its capacity. Under these circumstances, not only is the exogenous metabolism used in such a way that tissue repair takes place with great rapidity, as is shown by the remarkable increase in weight which patients often show during convalescence, but the endogenous metabolism, with which we assume creatinin to be associated, is reduced as far as possible. We should, therefore, expect with the onset of convalescence a marked reduction in the creatinin output to occur, a deduction which is borne out by the facts.

Creatin—Quite as much, if not more, interest from the standpoint of pathological metabolism is attached to the presence of creatin in the urine. Physiologically, only one condition is known where it appears. This is starvation. On the withdrawal of food, and indeed even in malnutrition, creatin may appear in the urine. This has been shown by Benedict and Dieffendorff and by Cathcart in man, and by one of us in animals. To what its appearance is due it is impossible to say. It is supposed to arise from the breaking down of muscle whose protein is being catabolized. On the other hand, one would scarcely expect it to appear in conditions in which the body was eager to utilize all the available nitrogen-containing compounds possible, for Folin, Klercker and Shaffer, with one of us, have shown that creatin given by mouth on a diet containing little or no protein is utilized as a foodstuff, and not all the nitrogen appears in the urine, but part is stored up in the body. Hence its appearance in the urine in starvation and in these pathological conditions is not connected with starvation alone, for the creatin must be formed at a point when the processes which transform ingested creatin into tissue nitrogen are unable to attack it. Hence it escapes and is excreted in the urine. That it is connected with certain unknown pathological processes seems certain. One finds during the stage of hyperpyrexia that the creatin output is high, despite the fact that the patients are receiving a diet which under normal conditions, both in heat units and nitrogen content, is amply sufficient to protect the urine from the appearance of creatin. Moreover, during convalescence the urine of a patient on the same diet will be perfectly free from creatin. It will be noted that the urine of the patient under discussion, whose case was clinically one of a mild type, contained no creatin, except on a single day in which there was a slight postcritical rise in temperature.

Uric Acid—Compared with the results obtained from normal subjects, the uric acid output throughout this case is high. Folin (24), in his averages of 30 normal urines, gives the highest output for uric acid nitrogen as 0.15, the lowest 0.08 gm., and the average 0.12 gm. During this time the patient was defervescing, the uric acid nitrogen varied from 0.38 to 0.24, and on the day before the postcritical rise 0.55 gm. of uric acid nitrogen were eliminated. From that time on the uric acid excretions fell rapidly until on the 25th it was 0.08 gm., the lowest value recorded by Folin. It will be noted that the highest output, 0.55 gm., occurred on the 23d. This is four days after the normal temperature had been reached for the first time, but also on a day on which an excessive nitrogen excretion was obtained. On this day, therefore, it would appear that the autolytic products, resulting from resolution of

the lung and containing much nuclein derivatives, were thrown into the circulation and incompletely catabolized.

Rest Nitrogen—One of us in several papers already published has indicated that rest nitrogen plays an important part in the scheme of analysis here followed. In certain disease, notably typhoid fever, and the toxemias of pregnancy, it has been found in the severer stages of the condition that the relative and absolute amounts of the rest nitrogen fractions are increased. This we have been disposed to set down to defective processes of desamidation. It is, therefore, interesting to compare the present series of examinations in pneumonia with typhoid fever, as the two have the common factors of high temperatures, loss of nitrogen and of body weight. One finds in the severe cases of pneumonia extremely high absolute amounts of undetermined nitrogen, but the relation of rest nitrogen to total nitrogen urea never reached the high value one observes in typhoid fever and eclampsia.

The maximum figure for normal subjects which Folin gives is 0.85 gm. and the lowest 0.41 gm., as against, in the mild cases, 1.93 gm. On the other hand, while the ratio for undetermined nitrogen varied in the normal urine of Folin from 2.7 per cent. to 5.3 per cent., the values in this case are not a great deal higher. On the first day of the examination, it is true, 8.9 per cent. of the total nitrogen was excreted in this form; on the following days the ratio was 2.1 to 7.8 per cent.

One may say, therefore, that, while a large amount of undetermined nitrogen is eliminated, even in the milder cases of pneumonia, the ratio of this fraction of the nitrogen rises but little, if at all. It is, however, signficant that when the stage of apyrexia and convalescence has set in, the absolute amounts of undetermined nitrogen are entirely within the limits of what is found for normal subjects. It has been observed on numerous occasions that during the resolution of the lung albumose-like substances have been excreted in the urine, due, as it is thought, to the entrance into the circulation of the products of the autolysis of the lungs. These would naturally be found in the rest nitrogen fraction. In some cases (Nos. 1, 4, 5, 9 and 13) we have tested for the presence of albumoses by Devoto's modification of Hofmeister's method. We have never found such amounts of albumoses as would account for the very high amounts of rest nitrogen found in this case and the following.

The Sulphur and Its Partition—As we have already mentioned, the excretion of sulphur and its reation to nitrogen should afford a valuable indication of the type of protein catabolized. It is well known that the relation of sulphur to nitrogen in protein varies between very wide limits. If at a definite time the type of nitrogen catabolized should change, one should have evidence of this change in the varying relation of sulphur to nitrogen in the urine.

If one recalculates the values obtained by Folin in his work on normal urine, one finds a remarkably close agreement between his normal, high, low and average ratios. These are, respectively, 8.3, 8.2 and 8.2, and by dividing the lowest sulphur by the highest nitrogen, and the highest sulphur by the lowest nitrogen, we obtain extreme values of 7.2 and 10 per cent. In the case which we are at present discussing the ratios are undoubtedly lower, varying between 7.4 and 5.1 per cent. This does not always hold, as will be seen in other cases, but from a study of the tables an impression will be gained that at high temperatures the body seeks to retain those proteins containing the higher amount of sulphur, and, for this reason, the ratio of sulphur to nitrogen in the urine falls.

This phenomenon is also to be observed, to a certain extent, in starvation. In this instance, when the body has obvious need of sparing its most valuable protein, and uses up the lesser type, the ratio also falls.

Sulphate Sulphur—One has been accustomed for many years to assign the formation of sulphates, particularly the alkaline sulphates, to much the same class of processes as those giving rise to urea, and both have been regarded as indications of the oxidative capacity of the organism. We know that the urea-forming function is not in any sense an oxidation. With the sulphur, however, one must admit that oxidation is the process taking place in transforming the cystin group of the protein molecule into sulphates. This fact Zweifel has used, not with very great success, as a basis to prove a condition of suboxidation occurring in eclampsia.

In the present case, no question of "suboxidation" can be raised, for the ratios of total sulphate sulphur to the total sulphur are high, exceptionally so. The minimum and maximum figures in Folin's results were 84.7 and 89.6 per cent. Here we find ratios between 85.0 and 92.8 per cent. It is notable that the highest value comes upon the day of highest nitrogen output, when 30.1 gm. of nitrogen were excreted.

Ethereal Sulphate Sulphur—The values for ethereal do not call for any especial comment in this case. In none of the cases examined are the amounts of ethereal sulphur excreted beyond those found in normal subjects. In Folin's analyses, the

absolute amounts of etheral sulphur excreted varied between 0.076 and 0.100, the average being 0.088. The amounts excreted by this patient were decidedly below this. This is in spite of the fact that the urine showed marked reactions for indican. One of us has previously shown in experimental work in animals that the excretion of ethereal sulphur bears no relation to the test of indican, and this is borne out in cases of pneumonia. It is shown extremely well in this case. One finds a marked test for indican on a day (24th) on which the ethereal sulphur excretion was 0.05 gm., and a weak test on the 21st, on which day 0.06 gm. were excreted.

The Neutral Sulphur—This fraction of the sulphur deserves especial consideration, for the reason that, apart from being concerned with processes of endogenous metabolism, a comparison of the neutral sulphur with the undetermined nitrogen should throw light on the composition of the latter. In the group of compounds designated as rest nitrogen, there are estimated the purin compounds, excluding uric acid, the proteic acids of Bondzynski and his coworkers, the amino-acids, indol and skatol compounds, etc. The compounds which interest us here are the proteic acids which contain sulphur, and hence are common to the rest nitrogen and neutral sulphur groups. Most of the albumoses also contain sulphur and are hence in these two classes. As has been mentioned, albumoses are found in the urine in pneumonia, particularly during the stage of resolution, and Gawinski (25) has found that the proteic acids are found increased in certain pathological conditions.

A consideration of the relation of neutral sulphur to undetermined nitrogen should enable us to determine whether at certain periods of the disease relatively more sulphur-containing compounds of unknown character are excreted.

In the case under examination it will be seen that the ratios vary considerably. Starting with a ratio of neutral sulphur x 100 to rest nitrogen of 13.2 on the day of a beginning crisis, the ratio suddenly rises to 46.3, a phenomenon which would correspond with Gawinski's findings of increased oxyproteic acids. Thereafter the ratio falls to the neighborhood of 10 per cent. (8.9; 7.8; 9.0), and on the last day of the examination rises to 26.4 per cent. In some of the following cases much greater differences will be found in the ratios between the neutral sulphur and undetermined nitrogen, and one case will furnish an example of as much sulphur in neutral form being excreted as rest nitrogen.

Phosphorus—In connection with the breaking down of nuclear compounds and their metabolism, the phosphorus elimination shows a marked rise during the latter part of the crisis. Not only is the rise an absolute one, but the ratio to total nitrogen is increased over 300 per cent. It would appear, from this case at least, that during the stage of hyperpyrexia phosphorus is retained by the body in much the same way as is the chlorin. This agrees entirely with Gouraud's statement (26). In Gouraud's case the commencing increase in the chlorin excretion preceded that of phosphorus by twenty-four hours.

During the first period of the examination of the present case but 0.06 gm. of chlorin were excreted. This was followed by a rise to 0.22 gm., while the excretion of phosphorus remained constant, rising on the succeeding day. Gouraud was not able to make out a coincidence between the excretion of chlorin and phosphorus, nor, as will be seen from our results, have we.

Case 2—The patient, T. E. S., male, 23 years of age, non-alcoholic, was admitted on the third day of the disease (January 26) with a mild attack of right lower lobe pneumonia. His general condition was excellent; he never gave the impression of being ill. February 2 the temperature began to fall, patient slept well, ate well, and was comfortable; same on the 28th, with temperature two degrees lower. On the 29th temperature reached normal. Convalescence from then on was uninterrupted.

The examination of the metabolism of this patient was commenced during the crisis. The temperature of the patient was falling already on the day of admission.

This case differs from the preceding in that the increase in nitrogen in Case 1 was not arrived at until the third day after the temperature was normal. There is also to be noted the marked fall in nitrogen excretion at the end of the experiment, when the patient came into what was practically nitrogenous equilibrium on a diet on which but a few days before he had lost nearly 20 gm. of nitrogen.

Creatinin and Creatin—In acordance with the clinical findings of a not excessively toxic condition, the creatinin elimination is not high, but a not inconsiderable amount of creatin is excreted, the results showing an almost constant daily quantity throughout the disease. On the day of highest nitrogen elimination, the creatinin was very high for this patient (0.52 gm.), falling on the subsequent days to the original excretion, 0.31 gm. As probably on this day a large amount of nitrogen, due to the resolution of the lung, was thrown into the circulation, it is suggestive that a part of this creatinin was derived from the products of autolysis.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Per Cent. T. S.	Chlorin. Gm.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
2	832	1024	+	0	0	15					
3	628	1025	+	0	0	15	2.4	0.60	1.10	15.1	100–88	103.6–101.9
4	1110	1023	+ +	0	0	27	5.1	0.19	0.30	16.3	120–92	101.4–100.5
5	635	1025	+	+	0	13	7.5	0.27	0.39	19.9	110–92	100. – 98.4
6	535	1021	+	0	0	10	1.8	0.85	0.62	19.8	96–80	99.8– 99.0
7	570	1016	+	0	0	6	2.8	0.71	0.53	14.4	96–78	99.4– 98.4
							1.8	0.65	0.42	15.2	104–80	100. – 98.4

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Chlorin.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.				
3	1530	1021	+	0	+	22.	6.96	0.91	30.7	98–84	103.6–103.0
4	940	1018	+	+	0	9.	5.18	0.38	11.7	108–80	103.6–102.8
5	650	1019	+	+	+ *	7.	2.71	0.49	24.5	104–88	103.4–102.0
6	390	1023	+	+	+ *	5.	1.61	....	30.4	108–98	103.8–102.8
7	380	1022	+	0	+	5.	0.53	....	40.8	104–96	103.4–101.2
8	....	1030	+	0	+	....	....	....	....	104–82	102.8–102.0
9	1370	1006	+	0	+	5.	3.49	0.22	104.2	110–88	102.4–101.0
10	3680	1001	+	0	0	4.	4.68	0.21	131.8	100–84	103.2– 99.8

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
								Gm.	Gm.		
2	2040	1014	+	0	+ + +	4	16.9	5.7	1.22	1.96	112–84	104.0–101.0
3	2500	1008	+	0	+	2	18.3	25.9	1.30	2.45	96–72	101.8–100.0
4	2455	1011	+	0	+ + + +		14.1	22.3	1.75	0.88	76–64	99.2– 98.4
5	1870	1012	+	0	+ + +		13.3	28.1	1.76	1.79	64–60	99.0– 98.2
6	1190	1019	+	0	+ +		9.8	27.0	1.33	3.35	64–60	99.0– 98.0
7	960	1030	+	0	+ +		9.6	12.2	1.49	2.31	76–64	98.6– 98.0
8	1105	1017	+	0	+ + + +		12.5	31.2	1.08	1.25	80–64	98.4– 98.2
9	940	1018	+	0	+ +		14.5	37.5	0.62	1.08	72–64	98.4– 98.0
10	1145	1019	+	0	+		8.7	19.5	1.22	2.30	68–64	98.4– 98.0
11	1930	1022	+	0	+ +		9.4	18.2	2.56	4.55	84.64	98.8– 98.0
12	660	1016	+ +		+		14.3	64.3	0.82	0.32	92–72	99.0– 98.4
13	480	1021	+	0	+ + + +		10.5	37.5	0.66	0.57	96–92	99.0– 98.4

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.		Gm.	Gm.		
7	625	1021	+	0	+ + +	13.	5 19.8	0.23	0.64	108–80	102.8–98.4
8	345	1024	+	0	+ + +	7.	5 6.8	0.18	0.20	84–72	100.0–98.0
9	390	1028	+	0	+ + +	9.	5 7.1	0.44	0.24	80–78	99.0–98.0
10	855	1021	+	0	+ + +	12.	5 8.4	0.92	2.82	76–68	98.0–97.8

TABLE 2.—PROTEIN METABOLISM IN CASE 2. MILD PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Ammi Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Chlorin.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.							
1	832	1024	+	0	0	15.91	14.11	88.7	1.09	6.9	13.02	81.8	0.32	2.0	0.25	1.6	0.04	0.3	1.19	7.4	1.45	9.1	1.27	87.6	1.24	85.8	0.03	2.1	0.18	12.4	0.60	1.10	15.1	100–88	103.6–101.9
2	628	1025	+	0	0	15.14	13.42	88.7	0.69	4.5	12.74	84.2	0.28	1.9	0.23	1.5	0.04	0.3	1.16	7.6	1.26	8.3	1.07	84.9	1.03	81.7	0.04	3.2	0.19	15.1	0.19	0.30	16.3	120–92	101.4–100.5
4	1110	1023	+	+	0	27.57	24.84	90.2	2.14	7.8	22.70	82.4	0.52	1.9	0.19	0.7	0.06	0.2	1.96	7.0	2.23	8.1	1.84	82.5	1.78	79.8	0.06	2.7	0.39	17.5	0.27	0.39	19.9	110–92	100. – 98.4
5	635	1025	+	+	0	13.69	11.92	87.2	2.73	20.0	9.19	67.2	0.30	2.2	0.23	1.6	0.04	0.3	1.21	8.7	1.10	8.0	0.86	78.2	0.82	74.5	0.04	3.7	0.24	21.8	0.85	0.62	19.8	96–80	99.8– 99.0
6	535	1021	+	0	0	10.10	8.51	84.1	0.64	6.3	7.87	77.8	0.27	2.7	0.09	0.9	0.02	0.2	1.11	11.1	0.70	6.9	0.54	77.2	0.48	68.6	0.06	8.6	0.16	22.8	0.71	0.53	14.4	96–78	99.4– 98.4
7	570	1016	+	0	0	6.82	5.63	82.5	0.59	8.6	5.04	73.9	0.31	4.5	0.06	1.0	0.03	0.5	0.79	11.6	0.55	8.1	0.43	78.2	0.37	67.3	0.06	10.9	0.12	21.8	0.65	0.42	15.2	104–80	100. – 98.4

TABLE 3.—PROTEIN METABOLISM IN CASE 3. MILD PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Ammi Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Chlorin.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.							
3	1530	1021	+	0	+	22.80	20.06	88.0	1.66	7.3	18.40	80.7	0.78	3.4	0	0	0.30	1.4	1.66	7.2	1.92	8.4	1.41	73.4	1.33	69.3	0.08	4.1	0.51	26.6	6.96	0.91	30.7	98–84	103.6–103.0
4	940	1018	+	+	0	9.88	8.25	83.6	0.45	4.6	7.80	79.0	0.43	4.4	0	0	0.10	1.0	1.03	10.3	0.70	7.1	0.58	82.9	0.53	76.8	0.05	6.2	0.12	17.1	5.18	0.38	11.7	108–80	103.6–102.8
5	650	1019	+	+	+	7.96	6.23	78.3	0.76	9.5	5.47	68.8	0.45	5.8	0	0	0.10	1.2	1.18	14.7	0.65	8.2	0.36	55.4	0.30	46.2	0.06	9.2	0.29	44.6	2.71	0.49	24.5	104–88	103.4–102.0
6	390	1023	+	+	+	5.50	4.25	77.3	0.54	9.8	3.71	67.5	0.36	6.5	0	0	0.10	1.8	0.79	14.4	0.46	8.4	0.22	47.8	0.19	41.3	0.03	6.5	0.24	52.2	1.61	.....	30.4	108–98	103.8–102.8
7	360	1022	+	0	+	5.45	4.24	77.8	0.41	8.0	3.80	69.7	0.40	7.8	0	0	0.10	1.9	0.79	13.5	0.51	9.4	0.22	43.4	0.18	35.3	0.04	7.8	0.29	56.9	0.53	.....	40.8	104–96	103.4–101.2
8	.....	1030	+	0	+	.....	.....	77.3	.....	7.0	.....	70.3	.....	7.6	0	0	.....	.....	.....	15.1	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	104–82	102.8–102.0
9	1370	1006	+	0	0	5.78	5.10	88.2	0.71	12.3	4.39	76.0	0.37	6.4	0	0	0.07	1.2	0.24	4.2	0.47	8.1	0.22	47.1	0.20	43.3	0.02	3.8	0.25	52.9	3.49	0.22	104.2	110–88	102.4–101.0
10	3680	1001	+	0	0	4.53	3.83	84.5	0.85	18.7	2.98	65.8	0.32	8.2	0	0	0.11	2.4	0.32	4.9	0.48	10.6	0.19	39.6	0.14	29.1	0.05	10.5	0.29	60.4	4.68	0.21	131.8	100–84	103.2– 99.8

TABLE 4.—PROTEIN METABOLISM IN CASE 4. MILD PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Ammi Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.						
2	2040	1014	+	0	+ + +	24.84	19.80	79.7	0.75	3.0	19.05	76.7	0.55	2.2	0.00	0.0	0.28	1.1	4.21	17.0	1.42	5.7	1.18	83.1	1.12	78.9	0.06	4.2	0.24	16.9	5.7	1.22	1.96	112–84	104.0–101.0
3	2500	1008	+	0	+	17.33	15.07	91.0	1.00	5.8	14.39	83.8	0.48	2.8	0.00	0.0	0.11	0.7	0.85	4.9	1.30	6.9	0.98	81.7	0.84	78.3	0.04	3.4	0.22	18.3	25.9	1.30	2.45	96–72	101.8–100.0
4	2455	1011	+	+	+ + +	21.41	19.60	91.5	1.30	6.1	18.30	85.4	0.54	2.5	0.00	0.0	0.17	0.8	0.94	4.4	1.49	6.9	1.28	85.9	1.25	83.6	0.03	2.0	0.21	14.1	12.3	1.75	0.88	76–64	99.2– 98.4
5	1870	1012	+	+	+ + +	17.60	16.32	92.8	0.94	5.3	15.38	87.3	0.49	2.8	0.00	0.0	0.22	1.2	0.57	3.2	1.20	6.8	1.04	86.7	0.98	81.7	0.06	5.0	0.16	13.3	28.1	1.76	1.79	64–60	99.0– 98.2
6	1190	1019	+	+	+ + +	16.30	15.33	94.0	2.16	13.3	13.17	80.7	0.48	2.9	0.00	0.0	0.13	0.7	0.32	2.4	1.02	6.3	0.92	90.2	0.86	84.4	0.06	5.9	0.10	9.8	27.0	1.33	3.35	64–60	99.0– 98.0
7	960	1030	+	+	+ +	16.76	15.42	93.0	0.50	3.0	14.92	89.0	0.46	2.7	0.00	0.0	0.06	0.4	0.82	4.9	1.04	6.2	0.94	90.4	0.87	83.7	0.07	6.7	0.10	9.6	13.2	1.49	2.31	76–64	98.6– 98.0
8	1105	1017	+	+	+ + +	13.48	12.58	93.3	0.78	5.8	12.30	91.2	0.41	3.0	0.00	0.0	0.17	1.3	0.32	2.4	0.80	6.0	0.70	87.5	0.67	83.8	0.03	3.7	0.10	12.5	31.2	1.68	1.25	80–64	98.4– 98.2
9	940	1018	+	+	+	9.89	9.16	92.7	1.36	13.8	7.80	78.9	0.29	2.9	0.07	0.7	0.13	1.3	0.24	2.4	0.62	6.3	0.53	85.5	0.49	79.0	0.04	6.5	0.09	14.5	37.5	0.63	1.08	72–64	98.4– 98.0
10	1145	1009	+	0	+	10.90	10.09	92.7	1.36	9.7	11.56	83.2	0.46	3.3	0.00	0.0	0.06	0.5	0.46	3.3	1.03	7.4	0.94	91.3	0.91	88.3	0.03	3.0	0.09	8.7	19.5	1.22	2.30	68–64	98.4– 98.0
11	1930	1022	+	0	+ + +	18.97	16.89	92.9	0.87	3.0	16.15	85.1	0.55	2.9	0.00	0.0	0.25	1.3	0.68	3.6	1.43	7.5	1.26	88.1	1.20	84.4	0.03	2.1	0.20	11.9	25.6	1.56	4.55	84–64	98.8– 98.0
12	660	1016	+	+	+	8.22	7.77	94.6	0.31	3.8	7.46	90.8	0.22	2.6	0.04	0.5	0.05	0.6	0.14	1.7	0.63	7.6	0.54	85.7	0.51	81.0	0.03	4.7	0.09	14.3	6.84	0.82	0.33	92–72	99.0– 98.4
13	480	1021	+	0	+ + + +	8.11	7.60	93.7	0.18	2.2	7.42	91.5	0.22	2.7	0.05	0.6	0.08	0.9	0.16	2.1	0.57	7.0	0.51	89.5	0.48	84.2	0.03	5.3	0.06	10.5	37.5	0.66	0.57	96–92	99.0– 98.4

TABLE 5.—PROTEIN METABOLISM IN CASE 5. MODERATELY SEVERE PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Ammi Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.						
7	625	1021	+	0	+ + +	13.44	12.03	89.5	0.47	3.5	11.56	86.0	0.27	2.0	0.00	0.0	0.23	1.7	0.91	6.8	0.88	6.5	0.70	79.5	0.66	75.0	0.04	4.5	0.18	20.5	19.8	0.23	0.64	108–80	102.8–98.4
8	345	1024	+	0	+ + +	7.31	6.20	86.0	0.31	4.3	5.89	81.7	0.13	1.8	0.00	0.0	0.14	1.9	0.74	10.3	0.40	5.6	0.35	87.5	0.31	77.5	0.04	10.0	0.05	12.5	6.8	0.18	0.20	84–72	100.0–98.0
9	390	1028	+	0	+ + +	9.60	7.93	88.1	0.37	4.1	7.56	84.0	0.16	1.8	0.00	0.0	0.07	0.8	0.84	9.3	0.52	5.8	0.46	88.5	0.43	82.7	0.03	5.8	0.06	11.5	7.1	0.44	0.24	80–78	99.0–98.0
10	855	1021	+	0	+ + +	12.70	11.37	89.5	0.48	3.8	10.89	85.7	0.29	2.3	0.00	0.0	0.21	1.6	0.83	6.6	0.74	5.8	0.67	90.5	0.62	83.8	0.05	6.7	0.07	9.5	8.4	0.92	2.82	76–68	98.0–97.8

It will be noted that while the creatin output is high in the first part of the examination, no increase takes place with increase in total nitrogen, and, following this, the substance all but disappears from the urine.

Uric Acid—The uric-acid excretion in this case is somewhat anomalous, for the amount excreted during the disease is, if anything, below that found in normal subjects, and no rise takes place in its excretion during the period in which a very large amount of nitrogen is being catabolized. During the period from the 28th day to the 31st, the leucocyte count fell from 24,100 to 10,000 per cubic millimeter. The remaining point in connection with this case is the close relation which exists between the neutral sulphur and the undetermined nitrogen. No such variation takes place as was found in Case 1. The values in the present case lie between 15 per cent. and 20 per cent., while in the former case a variation occurs between 7.8 per cent. and 46.3 per cent. One may conclude in this case that with regard to their sulphur content the substances which were being excreted as undetermined nitrogen were fairly constant in composition.

Case 3—The patient, B., male, 45 years of age, three days before admission had pain in the right side with shortness of breath and very slight cough. He did not have a chill, but sweated at night. Examination showed over the middle and right middle lobes anteriorly and laterally very loud pleuritic friction sounds; over right lower lobe posteriorly and laterally marked dullness, diminished fremitus and diminished distant breathing. Diagnosis, pleurisy with effusion. The patient was given the non-nitrogenous diet, consisting of malted starch, cream and sugar, and 6 gm. of sodium chlorid.

This third case, which serves to a certain extent for comparison with the foregoing two, is one of tuberculous nature with continued high temperature. As will be seen from the records, the temperature was seldom under 103, and for a greater part of the time of the examination 104. With this temperature there was no hyperleucocytosis, and the Widal reaction was negative. Before the examination, 1.000 c.c. of fluid had been taken from the chest.

This patient is of interest also from the dietetic side, for he was given a nearly non-nitrogenous diet (27), consisting of malted starch (28) and cream. The number of calories given were 2,500. The nitrogen content of the food was about 1 gm. In addition, 6 gm. of sodium chlorid were administered.

On the first day of the examination 22.8 gm. of nitrogen were excreted in the urine, representing at least that amount of nitrogen loss from the body. Thereafter the amount fell 9.8, and finally to 4.5 gm.

This lower amount is what one may obtain in a normal individual with the same diet, so that even with the high temperature of this patient (103.6 on the sixth day) an output of 4.53 gm. cannot be considered as the indication of a very definite toxic destruction of protein.

This case will later be compared with that of a highly toxic pneumonia patient (Case 12), who was placed for a few days on this diet. The most striking differences in the reaction of the two cases to this diet will be at once apparent.

Throughout this case was observed a very close agreement with the normal ngures of Folin. Moreover, no creatin is found at any time in this series of analyses, despite the fact that during the examination the patient received practically no protein.

On the last day on which the urine was examined, a marked polyuria will be noted, due to the administration of 1,000 c.c. of "white drink."

The flushing out of the system by the very large quantity of urine passed did not have any influence either on the excretion of nitrogen or on the undetermined nitrogen.

Case 4—The patient, L. B., male, 18 years of age, was admitted on the fifth day of the disease (April 26) with a mild attack of central pneumonia, coming to the surface of the lung at the lower right lobe in small area. On the 27th the patient was comfortable, condition good. A precritical rise of temperature to 104 occurred on this day, followed on the 28th by defervescence during the day, which was completed on early morning of the 29th. On the 28th he was comfortable, condition excellent; on the 29th, lung was resolving, which was completed by May 1. Convalescence was uninterrupted; patient discharged May 10.

In this case the crisis occupied about thirty-six hours for its completion, and in order to study the effects of an uninterrupted convalescence the examinations of the urine were continued over nine days, during which time the temperature was normal. One finds the nitrogen and sulphur excretion steadily decreasing, but the total output is high, never decreasing below 9.89 gm. This is in marked contrast with the case of pleurisy (Case 3, B.) which we have just discussed.

On the eleventh day of the disease there is a marked rise in the nitrogen excretion to 28.9 gm., unaccompanied by rise in temperature, pulse or any unusual clinical signs. Unquestionably, at this point the products of the autolysis of the pulmonary exudate were suddenly thrown into the circulation. On the day preceding, warning of this was given by a rise in total nitrogen from 9.8 to 13.9 gm. This rise is not accompanied by any special features in the distribution of the nitrogen, except in two respects, a marked rise in the excretion of creatinin, and the advent of a comparatively large amount of creatin in the urine. Unexpectedly, the uric-acid excretion is not affected, although on this day a very large amount of phosphorus is eliminated. The reason for this is obscure. On this day, and the following day, the ratios of sulphur nitrogen undergo another change. Where for some time previously the ratios varied from 6.0 to 6.3, the ratio is now 7.4 to 7.6, indicating with this rise in the ratio that a type of protein is being catabolized which contains considerably more sulphur.

Regarding the ratio of neutral sulphur to rest nitrogen, some very interesting facts are disclosed bearing on the composition of these substances.

The high elimination of nitrogen at the crisis is attended with the excretion of substances of unknown composition, which are relatively poor in sulphur. The character of these substances changes directly after the crisis, when substances comparatively rich in sulphur are excreted.

The high postcritical rise in nitrogen excretion produces a group of nitrogenous substances which for two days are practically constant in their undetermined nitrogen-sulphur composition, the ratio standing at 5 to 1. This is followed by an exceedingly low excretion of rest-nitrogen compounds very rich in sulphur.

It is to be hoped that further work in the more detailed analysis of the rest nitrogen in conditions such as pneumonia will reveal the cause of this very interesting change in relationship.

Moderately Severe Cases.

Case 5—The patient, W. W., male, 25 years of age, not alcoholic, had right upper lobar pneumonia. He was admitted April 11 with frank moderately severe attack. On the third day of disease temperature was 104.5 F., pulse 102, respiration 36, during the night. The patient's general condition improved, and on the 12th he was in good condition. On the 13th he was slightly delirious during the day and night, but during the 14th he again improved, and on the 15th, the seventh day of the disease, he was comfortable and defervesced. The 16th, 17th, 18th and 19th were days of a rapid and good convalescence.

This case ended by crisis, with a marked postcritical rise on the day following. This day is the one on which the urine was first examined. This case does not differ markedly from the preceding case, except that the ratios for amid and urea nitrogen are somewhat higher. The ammonia is low, both relatively and absolutely, as is also the creatinin.

In this case one sees very clearly the retention of phosphorus and its subsequent elimination, after the temperature has reached normal.

Case 6—The patient, T. R., male, 46 years of age, moderately alcoholic, with history of syphilis, was admitted on fifth day of disease, though the lung was not fully consolidated. Temperature, 5 p. m., was 105 F., pulse 106, respiration 34. Consolidation developed during the night of admission in the right lower lobe. On the 21st patient was comfortable except for pain on coughing, condition good; moderately severe attack. On the 22d, condition was slightly better; on the 23d, condition showed continued improvement, and defervescence occurred during the night; on the 24th, improvement continued and resolution of lung began; on the 25th, resolution continued with marked general improvement; on the 26th, the patient was convalescent, lung resolved rather slowly.

This case differs from the preceding in that the defervescence was spread over at least four days. The analyses of the urine of the patient are complicated by the fact that on one day at least the urine was contaminated, and all the specimens but one were alkaline, so that the relative values for urea and ammonia are uncertain.

The case is of interest in showing postcritical rise in the elimination of nitrogen; on the 23d day, only 12.8 grams of nitrogen were excreted, while on the 25th day 24.2 grams were eliminated.

Very high ratios of total sulphur, total nitrogen were obtained on the second and third days of the examination, viz., 11.1 and 10.8, and in this respect this patient differs from the preceding ones, in which the effort of the individual to spare his sulphur at the beginning of the illness is made plain by the low ratio obtaining at that time.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm		Gm.	Gm.		
2	1000	1018	+	+	0	17.0	18.9	0.66	0.24	116– 96	103.8–103.4
3	520	1019	+	+ +	0	7.3	14.7	0.19	0.22	112–100	103.0–100.8
4	885	1016	+	0	0	12.8	13.7	0.29	0.11	120–100	103.2–100.4
5	1250	1017	+	0	0	22.8	13.0	0.37	0.38	106– 92	99.4– 98.2
6	1545	1019	+	0	0	24.7	14.5	1.34	0.75	92– 80	100.8– 99.4

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.		Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
								Gm.	Gm.		
4	1176	1023	+	+ +	+ +	25	20.1	0.62	1.06	116– 92	103.8–102.0
5	1150	1021	+	+ +	+ + +	19	25.0	0.68	0.83	120– 96	103.0–101.6
6	1100	1025	+	+	+ + + +	23	22.1	0.65	0.66	100– 92	102.2–100.4
7	700	1024	+	0	+ + + +	14	18.8	0.51	0.59	104– 92	102.4–100.2
8	560	1025	+	0	+ +	11	14.3	0.55	0.44	116– 88	102.0–100.2
9	No specimen received.										
10	710	1028	+	0	+ + + +	15	23.5	0.97	1.41	108– 96	102.2– 99.4
11	840	1027	+	0	+ + + +	17	21.2	1.13	1.82	108–100	102.6–100.6
12	960	1028	+	0	.....	20	12.2	1.46	1.61	96– 80	101.0–100.0

Table 6.—Protein Metabolism in Case 6. Moderately Severe Pneumonia.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			Gm.	Gm.		
2	1000	1018	‡	+	0	17.00	14.90	87.7	1.30	7.6	13.60	80.0	0.48	2.8	0.00	0.0	0.03	0.2	1.59	9.4	1.26	7.4	0.96	76.0	0.93	73.3	0.03	2.7	0.30	24.0	18.9	0.66	0.24	116– 96	103.8–103.4
3	520	1019	‡	++	0	7.39	6.07	82.1	2.81	38.0	3.26	44.1	0.12	1.6	0.09	1.2	0.02	0.3	1.09	14.8	0.82	11.1	0.67	81.1	0.65	79.0	0.02	2.1	0.16	18.9	14.7	0.19	0.22	112–100	103.0–100.8
4	895	1016	‡	+	0	12.80	10.76	84.1	1.81	14.2	8.45	66.9	0.14	1.1	0.34	2.7	0.03	0.2	1.53	11.9	1.38	10.8	1.17	84.9	1.13	82.0	0.04	2.9	0.21	15.1	13.7	0.29	0.11	120–100	103.2–100.4
5	1250	1017	‡	0	0	22.80	20.00	87.7	0.81	3.6	19.19	84.1	0.25	1.1	0.34	1.5	0.28	1.2	1.93	8.5	1.45	6.4	1.20	82.8	1.15	79.4	0.05	3.4	0.25	17.2	13.0	0.37	0.38	106– 92	99.4– 98.2
6	1545	1019	‡	0	0	24.72	21.48	86.9	6.63	26.8	14.85	60.1	0.23	0.9	0.35	1.4	0.03	0.2	2.61	10.6	1.55	6.3	1.17	75.5	1.13	72.6	0.04	2.9	0.38	24.5	14.5	1.34	0.75	92– 80	100.8– 99.4

Table 7.—Protein Metabolism in Case 7. Moderately Severe Pneumonia.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			Gm.	Gm.		
4	1176	1023	†	++	+	25.66	22.60	88.1	0.91	3.6	21.69	84.5	0.58	2.3	0.34	1.4	0.26	1.0	1.88	7.2	1.66	6.5	1.28	77.1	1.22	73.5	0.06	3.6	0.38	22.9	20.1	0.62	1.06	116– 92	103.8–102.0
5	1150	1021	†	++	+++	19.37	17.16	88.6	0.81	4.2	16.35	84.4	0.54	2.8	0.22	1.4	0.32	1.7	1.08	5.5	1.37	7.1	1.10	80.3	1.01	73.7	0.09	6.6	0.27	19.7	25.0	0.68	0.83	120– 96	103.0–101.6
6	1160	1025	†	+	++++	22.48	20.08	89.3	0.74	3.3	19.34	86.0	0.54	2.4	0.20	0.9	0.35	1.6	1.31	5.8	1.62	7.2	1.33	82.1	1.25	77.2	0.08	4.9	0.29	17.9	22.1	0.65	0.66	100– 92	102.2–100.4
7	700	1024	†	0	++++	14.76	13.08	88.6	0.83	5.6	12.25	83.0	0.48	3.2	0.00	0.0	0.34	1.6	0.96	6.6	1.02	6.9	0.84	82.4	0.77	75.5	0.07	6.9	0.18	17.6	18.8	0.51	0.59	104– 92	102.4–100.2
8	560	1025	‡	0	++	11.50	10.08	87.7	0.97	8.5	9.11	79.2	0.34	2.9	0.07	0.6	0.17	1.5	0.84	7.3	0.76	6.6	0.64	84.2	0.60	79.0	0.04	5.2	0.12	15.8	14.3	0.35	0.44	116– 88	102.0–100.2
	No specimen received.																																	
10	710	1028	†	0	++++	15.35	13.64	88.9	0.68	4.4	12.96	84.5	0.55	3.6	0.00	0.0	0.31	2.0	0.85	5.5	1.17	7.6	0.97	82.9	0.90	76.9	0.07	6.0	0.20	17.1	23.5	0.97	1.41	108– 96	102.2– 99.4
11	840	1027	†	0	++++	17.85	16.05	89.9	0.95	5.3	15.10	84.6	0.57	3.2	0.08	0.5	0.30	1.7	0.85	4.7	1.33	7.4	1.15	86.5	1.08	81.2	0.07	5.3	0.16	13.5	21.2	1.13	1.82	108–100	102.6–100.6
12	960	1028	†	0	.....	20.96	18.96	90.5	1.04	5.0	17.92	85.5	0.61	2.9	0.00	0.0	0.32	1.5	1.07	5.1	1.48	7.1	1.35	91.2	1.25	84.5	0.10	6.7	0.13	8.8	12.2	1.46	1.61	96– 80	101.0–100.0

Table 8.—Protein Metabolism in Case 8. Moderately Severe Pneumonia.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			
8	....	1025	†	+	..	.....	.....	95.6	.....	6.6	.....	89.0	.....	3.0	.....	0.0	.....	0.2	.....	1.2	126– 92	105.8–102.8
9	390	1027	‡	?	..	9.25	8.46	91.5	0.43	4.7	8.03	86.8	0.30	3.2	0.00	0.0	0.05	0.5	0.44	4.8	124–110	106.0–103.8
10	1045	1024	†	?	..	24.70	21.40	86.6	1.67	6.8	19.73	79.8	0.56	2.3	0.00	0.0	0.31	1.3	2.43	9.8	120– 90	104.0– 98.2
13	1425	1020	‡*	+	..	26.16	23.00	87.8	1.30	5.0	21.70	82.8	0.54	2.1	0.13	0.5	0.06	0.2	2.43	9.3	96– 70	100.0– 99.0

* Slightly alkaline. ? Trace.

Case 7—The patient, F—t, male, 26 years of age, non-alcoholic, was admitted on the first day of the disease, May 12. On admission temperature was 103, pulse 104, respiration 52. There were severe pain and dyspnea from pleurisy. The lung was in a stage of congestion in left lower lobe; the patient moderately sick. General condition was good on the 13th and 14th, though temperature was 104.5 F., pulse 120, respiration 24 during both afternoons; signs in chest seemed more those of fluid than consolidation. Chest was tapped with negative result. Patient was not so well during night of the 14th, decidedly improved on the 15th; moderately sick during the 16th. He continued to improve, and during the 17th to the 24th slowly but steadily improved. The temperature fell by lysis, the lung beginning to resolve on the 21st.

This case shows the course of a very protracted lysis, the temperature not reaching normal during the course of the examination. The diet during the examination contained four eggs, in addition to the amount the other patients received, bringing the nitrogen to 12 gm.

The first respect in which this case differs from the preceding is the constantly high excretion of nitrogen. The fluctuations are great, it is true, varying between 25.6 and 11.5 gm., but no steady decrease is observed in the elimination. It is instructive, however, to compare this case with Case 3, in which the temperature had a course similar to this except that the temperature was uniformly almost a degree higher. There we concluded we were dealing with a tuberculous pleurisy, with little or no toxic destruction of protein. Here, if one may judge from the nitrogen excretion, the amount of protein destroyed is excessive.

In accordance with what appears to us to indicate excessive metabolism due to the action of the toxins, one finds higher absolute amounts of creatinin with a fall at a period coinciding with lower temperature. With this high creatinin excretion, we find associated a large amount of creatin, reaching on the first day the very unusual amount of 0.34 gm. (29).

With the progress of the case, we here find a fall in creatinin and a subsequent rise and, what is of more interest, the practically complete disappearance of creatin from the urine. This case is also marked by the larger amount of uric acid excreted, a circumstance which seems also to point to excess in nuclear destruction. This is also partly borne out by the fact that the phophorus excretion in this case is uniformly high, in one day, the last of the examination, 1.46 gm. of phosphorus being excreted.

The next case which we present, while incomplete serially, gives the nitrogen metabolism occurring during a crisis in which the temperature fell in twenty-four hours from 106 to 98.2.

Case 8—The patient, P. F., male, aged 34, with alcoholic history, was admitted sixth day of disease, February 7, moderately sick, with a small central patch of pneumonia in the left upper lobe; symptoms in excess of amount of lung involved, with mild alcoholic hallucinations. In spite of high temperature (106), and pulse of 120, patient did not impress one as being very ill during the 18th and 19th. On the 18th consolidation spread through upper lobe. Rapid defervescence occurred on the 20th, and marked improvement; and on the 21st, convalescence. Lung cleared by the 25th.

The first collection of urine was not made quantitatively. On the day on which the crisis commenced, the total nitrogen was comparatively low, only 9.2 gm. being excreted. During the following twenty-four hours the nitrogen excretion had risen to 24.7 gm. With this increase the uric acid, previously excreted to the amount of 0.05 gm., rises to six times that amount. The undetermined nitrogen also increased in exactly the same ratio.

The crisis was followed by a slight postcritical rise, during which no more specimens of urine were examined. The excretion of nitrogen on this day was even higher, rising to 26.1 gm. In both these days the low ratio of amid nitrogen, and the high undetermined nitrogen, led one to conclude that through this period the products of autolysis were being excreted in such amounts as to escape the catabolic processes leading to ammonia and urea.

Severe Cases.

The following group of cases are those of patients clinically characterized as severely ill:

Case 9—The patient, C., male, 27 years of age, non-alcoholic, with history of syphilis four years previously, was admitted April 22 with right lower lobe pneumonia, eighth day of disease. On April 23, temperature was 104.8 F., pulse 104, respiration 40; patient was severely sick and delirious; general conditions not good. On the 24th, he was still severely sick. On the 25th, the patient began to improve, but was

still delirious. On the 26th, he was much improved in general condition, though still delirious; defervescence began. On the 27th, defervescence completed; general condition excellent, though patient was delirious at night. On the 28th, he was convalescent; on the 29th, lung cleared.

This case is distinguished from those which precede by a considerable amount of albumin in the urine, indicating the effect of the toxic condition on the kidneys. On the other hand, the toxemia does not appear to have led to a very marked destruction of protein, for at no point in the examination was the amount of nitrogen excreted excessive. We apparently have here an indication of two types of toxic condition, the one leading within the cell to a breaking down of protein and accompanied by a large amount of nitrogen in the urine; the other is shown by the irritative effect on the kidneys. As will be seen, in some of the most toxic cases which we have examined—cases which are recognized clinically as most severe—not only is the nitrogen output extremely high, but an intense nephritis is set up, as is shown by the large amount of albumin excreted in the urine.

With regard to the individual constituents of the urine, one notes the absolutely high uric-acid excretion during the period of highest temperature, the increase of creatinin after the critical fall in temperature, and during convalescence the disappearance of creatin from the urine. In this case, as in Cases 1 and 13, one observes the sudden change in the composition of the rest nitrogen, as indicated by the change in the ratio of undetermined nitrogen to neutral sulphur. On the days of lower nitrogen excretion, the ratio of neutral sulphur to rest nitrogen suddenly falls to 7.3 and 6.9, as against preceding ratios of 49.3 to 37.5.

The retention of phosphorus during the period of high temperatures, while not striking, is distinct, and as the case proceeds to convalescence there is a steady rise in the excretion of these substances.

Case 10—The patient, P. L., male, alcoholic, with left lower lobe pneumonia and influenza, was admitted on the third day of disease, January 10, in a serious condition; severely ill. On January 11, the patient was severely sick, but slightly easier and more comfortable, due to greater ease of breathing out of doors. On the 12th, condition same during the day, but at night the patient developed sudden delirium of alcoholic type. On the 13th, the general condition same except that delirium had diminished; 540 c.c. of semi-purulent fluid were drawn from the left chest. On the 14th, respirations were easier, but general conditions and delirium about the same; on the 15th, general conditions slightly but distinctly better; on the 16th, the patient was slightly better. On January 17, his general condition was much improved; mental condition normal; January 18, improvement continued; January 19, patient still improved. On January 20, general condition was not quite so good; signs of fluid had returned; on the 21st, the patient was not quite so well. On the 22d, conditions were good but not improving; 450 c.c. of bloody fluid drawn from the left chest. January 23, 24 and 25, conditions remained stationary. Operation was decided on the 25th, and on the 26th 200 c.c. of brownish, bloody pus were drained from chest. Patient's condition was good; January 27, it was improved, and from then on the patient made a slow but good recovery.

This case, one which must be regarded as a severe type of inflammation of the lung, is complicated by an empyema. The examination of the case is incomplete, for the reason that estimation of nitrogen content of the pyemic fluid was not made. During the examination the patient was tapped twice, and altogether 840 c.c. of pus removed.

The nitrogen is distributed more on the lines of a non-nitrogenous high carbohydrate diet, the ammonia ratio high, urea ratio low, and undetermined nitrogen high.

Apparently the condition was of such a type as to allow the nitrogen catabolism to be amenable to protection with carbohydrate.

It is also interesting to note that the ratio of neutral sulphur to undetermined nitrogen is very close to what Folin found in normal cases on a non-nitrogenous diet. For example, a recalculation of the lowest nitrogen output in Tables 7 and 5 of Folin's article gives a ratio of neutral sulphur to rest nitrogen of 20.0 and 15.4

With the exception of two days of distinctly high ratio, namely, 41.5, 31.2 and 25.0, the values found in the present case are practically within the normal figures given there; in other words, the rest nitrogen in this case appears to have a composition, as far as its content in sulphur goes, very close to what has been observed in the normal.

Case 11—The patient, F—d, male, 27 years of age, non-alcoholic, came to the hospital May 15, on the eighth day of disease, having been untreated; severely sick on admission. Temperature was 104, pulse 168, respiration 48. Next day, the 16th, the patient was still severely sick and delirious; on the 17th, he was distinctly better

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.			Gm.	Gm.		
2	1440	1013	+	+ + +	+ +	0.31	33.7	49.3	0.11	2.34	140–112	104.8–104.0
3	1220	1016	+	+ + +	+ +	0.37	32.2	35.0	0.51	1.24	130–102	104.8–102.2
4	905	1015	+	+ + +	+ +	0.24	27.9	37.5	0.15	0.65	120–100	105.0–101.8
5	1075	1017	+	+ + +	+ +	0.23	23.7	37.6	0.52	0.58	120– 92	102.4–100.6
6	910	1017	+	0	+ +	0.15	17.9	7.3	0.55	0.33	100– 80	99.2– 98.4
7	820	1020	+	+	+ +	0.16	17.4	6.9	0.85	0.25	90– 74	99.2– 98.0
8	450	1027	+	+	+ +	0.08	14.8	10.4	0.77	0.14	74– 64	98.0– 98.0
9	450	1026	+	0	+ +	0.08	15.4	10.0	0.62	0.17	60– 60	99.0– 98.0
10	600	1025	+	0	+ +	0.10	15.2	20.8	0.82	0.97	66– 66	98.0–.....
11	No urine received.											
12	1090	1016	+	0	+							
13	840	1020	+	0	+ +							
14	815	1025	+	0	+ +							
15	820	1028	+	0	+ +	0.08	9.5	12.3	1.01	3.59	74–...	98.0–.....
16	1100	1022	+	0	+ +	0.06	6.7	25.0	0.87	4.16	74–...	98.0–.....
17	940	1023	+	0	+ +	0.07	8.0	20.6	1.03	5.13	100–...	97.6–.....

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Neutral Sulphur.	Per Cent. S.	Chlorin.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
						Gm.		Gm.				
2	300	1023	+	+	+ +	0.13	39.4	0.69	0.08	18.0	136–120	103.0–101.8
3	350	1023	+	+ + +	+ +	0.17	44.7	0.49	0.18	41.5	126–122	102.2–100.0
4	785	1020	+	+	+	0.27	32.9	1.43	1.28	17.3	126–118	101.6–101.0
5	715	1020	+	+	0	0.25	44.6	1.43	0.21	15.6	126–120	102.2–101.2
6	380	1018	+	+	0	0.11	31.4	0.44	0.37	21.1	120–112	102.8–100.8
7	912	1012	+	+	0	0.20	31.7	0.72	....	31.2	120–110	102.0–100.4
9	670	1020	+	+	0	0.22	18.7	0.65	0.23	22.9	108–100	101.2–100.0
10	470	1021	+	+	0	0.17	18.1	0.40	0.42	25.0	120– 96	101.0–110.4
11	800	1015	+	+	+	0.21	31.3	0.54	0.47	21.6	120–102	102.2– 99.8
12	618	1017	+	+	+	0.20	39.2	0.38	0.72	12.5	116–102	101.6–100.6
13	905	1012	+	0	0	0.17	33.3	0.44	0.56	15.8	116–100	101.8–100.4
14	850	1014	+	0	0	0.21	47.5	0.62	0.51	14.8	116–100	101.4– 99.2
15	670	1013	+	0	0	0.13	32.5	0.40	0.40	13.2	110– 92	101.0– 99.8
16	820	1012	+	0	0	0.16	41.0	0.69	0.47	23.6	110–100	101.0– 99.8

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
								Gm.	Gm.		
2	845	1026	+	+	+	14.7	18.2	0.66	0.30	164–128	103.8–102.8
3	720	1027	+	+ +	+	12.6	16.7	0.66	0.04	112–104	103.0–101.2
4	800	1028	+	0	+ +	8.3	14.0	0.87	0.00	100– 88	100.4– 98.8
5	620	1029	+	0	+	11.3	21.8	0.73	0.15	96– 84	99.6– 98.4
6	730	1028	+	0	+					92– 76	99.2– 98.6
7	840	1027	+	0						96– 72	101.2– 98.8
8	630	1029	+	0	+	11.9	13.0	0.98	1.89	86– 72	99.6– 98.4
9	1040	1025	+	0	....	12.9	18.7	1.10	3.68	88– 76	99.2– 98.4
10	960	1020	+	0	....	14.0	24.5	1.12	2.07	88– 72	99.2– 98.4

Table 9.—Protein Metabolism in Case 9. Severe Pneumonia.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Albumin Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.						
2	1440	1013	†	++++	++++	12.39	0.55	10.15	87.1	0.83	7.1	9.32	80.0	0.53	4.6	0.03	0.3	0.32	2.7	0.63	5.3	0.92	7.5	0.61	66.3	0.53	57.6	0.08	8.7	0.31	33.7	49.3	0.11	2.34	140–112	104.8–104.0
3	1220	1016	†	++++	++++	14.39	0.23	12.26	86.5	1.11	7.8	11.15	78.7	0.51	3.6	0.05	0.4	0.28	1.9	1.06	7.6	1.15	8.0	0.78	67.8	0.71	61.7	0.07	6.1	0.37	32.2	35.0	0.51	1.34	130–102	104.8–103.2
4	905	1015	†	++++	++++	12.33	0.13	10.88	89.3	0.82	6.7	10.06	82.6	0.36	2.9	0.10	0.8	0.22	1.8	0.64	5.2	0.86	7.0	0.62	72.1	0.58	67.4	0.04	4.7	0.24	27.9	37.5	0.15	0.68	120–100	105.0–101.8
5	1075	1017	†	++++	++++	15.03	0.61	13.48	90.7	1.14	7.5	12.32	83.2	0.40	2.7	0.10	0.7	0.28	1.9	0.61	4.1	0.97	6.3	0.74	76.3	0.69	71.1	0.05	5.2	0.23	23.7	37.5	0.52	0.58	120–92	103.4–100.6
6	910	1017	†	0	++++	15.59	....	12.83	82.3	0.91	5.8	11.93	76.5	0.35	2.2	0.08	0.5	0.28	2.0	2.05	13.0	0.84	5.4	0.69	82.1	0.64	76.2	0.05	5.9	0.15	17.9	7.3	0.55	0.33	100– 80	99.2– 98.4
7	830	1020	†	0	++++	16.37	....	13.19	80.6	0.94	5.7	12.25	74.9	0.37	2.3	0.16	1.0	0.34	2.1	2.31	14.0	0.92	5.6	0.76	82.6	0.72	78.2	0.04	4.4	0.16	17.4	6.9	0.85	0.25	90– 74	99.2– 98.0
8	450	1027	†	0	++++	9.71	....	8.44	86.9	0.45	4.6	7.99	82.3	0.24	2.5	0.14	1.4	0.12	1.2	0.27	8.0	0.54	5.6	0.46	85.2	0.42	77.8	0.04	7.4	0.08	14.8	10.4	0.77	0.14	74– 64	98.0– 98.0
9	450	1026	†	0	++++	10.24	....	9.02	88.1	0.36	3.5	8.66	84.6	0.22	2.1	0.10	1.0	0.10	1.0	0.89	7.8	0.52	5.1	0.44	84.6	0.41	78.8	0.03	5.8	0.08	15.4	10.0	0.62	0.17	60– 60	99.0– 98.0
10	600	1025	†	0	+++	12.65	....	11.66	92.3	0.61	4.8	11.05	87.4	0.28	2.2	0.19	1.5	0.04	0.4	0.48	3.7	0.66	5.2	0.56	84.8	0.53	80.3	0.03	4.5	0.10	15.2	20.8	0.82	0.97	60– 66	98.0–.....
11	No urine received.																																			
12	1000	1016	‡	0	++	Urine decomposed.																														
13	840	1020	‡	0	++++	Urine decomposed.																														
14	815	1028	‡	0	++++	Urine decomposed.																														
15	820	1028	‡	0	++++	11.40	....	10.38	91.0	0.44	3.9	9.94	87.1	0.24	2.1	0.00	0.0	0.13	1.1	0.65	5.8	0.84	7.4	0.76	90.5	0.72	85.7	0.04	4.8	0.08	9.5	12.3	1.01	3.59	74–....	98.0–.....
16	1100	1022	‡	0	+++	11.78	....	11.31	96.0	0.32	2.7	10.99	93.3	0.19	1.6	0.00	0.0	0.04	0.3	0.24	2.1	0.89	7.6	0.83	93.3	0.77	86.6	0.06	6.7	0.06	6.7	25.0	0.87	4.16	74–....	98.0–.....
17	940	1023	‡	0	+++	11.03	....	10.30	93.5	2.29	20.8	8.01	72.7	0.26	2.4	0.00	0.0	0.12	1.1	0.34	3.0	0.87	7.9	0.80	92.0	0.75	86.2	0.06	5.8	0.07	8.0	20.6	1.03	5.13	100–....	97.6–.....

Table 10.—Protein Metabolism in Case 10. Severe Pneumonia.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Albumin Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. S.	Alkali Sulphate Sulphur.	Per Cent. S.	Ethereal Sulphate Sulphur.	Per Cent. S.	Neutral Sulphur.	Per Cent. S.	Chlorin.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.						
2	300	1023			+++	6.02	....	5.05	83.9	0.59	9.8	4.46	74.1	0.23	3.8	....	....	0.02	0.3	0.72	12.0	0.33	5.5	0.20	60.6	0.17	51.5	0.03	9.1	0.13	39.4	0.69	0.08	18.0	136–120	103.0–101.8
3	350	1023		+	+++	5.72	0.88	4.01	82.8	0.44	9.0	3.57	73.8	0.25	5.3	....	....	0.17	3.5	0.41	8.5	0.38	6.6	0.21	55.3	0.17	44.7	0.04	10.6	0.17	44.7	0.49	0.18	41.5	126–122	102.2–100.0
4	785	1020			sc	9.04	....	7.24	80.1	1.54	17.0	5.50	60.8	0.41	4.5	0.22	2.0	1.56	13.8	0.82	7.3	0.51	5.6	0.34	66.6	0.27	52.9	0.07	13.7	0.17	32.9	1.43	0.28	17.3	126–118	101.4–101.0
5	715	1020		0	+	8.04	....	5.91	73.5	1.24	15.4	4.67	58.1	0.42	5.2	0.07	0.9	0.04	0.5	1.60	19.9	0.56	7.0	0.31	55.4	0.27	48.2	0.04	7.2	0.25	44.6	1.43	0.21	15.6	126–120	102.2–101.2
6	380	1018		0	+	5.03	....	4.03	79.9	0.53	10.5	3.50	69.4	0.23	4.6	0.11	2.1	0.16	3.2	0.57	10.2	0.35	6.9	0.24	68.6	0.22	62.8	0.02	5.8	0.13	31.4	0.44	0.37	31.1	120–112	102.8–100.8
7	913	1013		0	+	7.95	....	6.44	81.0	0.94	11.8	5.50	69.2	0.38	4.8	0.17	2.1	0.32	4.0	0.64	8.1	0.63	7.9	0.43	68.3	0.39	61.9	0.04	6.4	0.20	31.7	0.72	....	31.2	120–110	102.0–100.4
8	670	1020		0	+	9.66	....	7.88	81.6	0.94	9.8	6.94	71.8	0.43	4.4	0.25	2.6	0.14	1.4	0.96	10.0	1.18	12.3	0.96	81.3	0.92	78.0	0.04	3.3	0.22	18.7	0.65	0.23	22.6	108–100	101.2–100.0
9	470	1021		0	+	7.33	....	6.18	83.7	1.09	15.0	5.04	68.7	0.27	3.7	0.14	1.9	0.11	1.5	0.68	9.2	0.94	12.8	0.77	81.9	0.73	77.7	0.04	4.2	0.17	18.1	0.40	0.42	25.0	120– 96	101.0–101.4
11	800	1015			+	8.94	....	7.26	81.2	0.56	6.3	6.20	74.9	0.35	4.0	0.16	1.8	0.20	2.2	0.97	10.8	0.67	7.5	0.46	68.7	0.40	59.7	0.06	9.0	0.21	31.3	0.54	0.47	21.6	120–102	103.2– 99.8
12	618	1017			+	7.73	....	5.46	70.7	0.64	8.3	4.82	62.5	0.33	4.3	0.17	2.2	0.17	2.2	1.60	20.6	0.51	6.6	0.31	60.8	0.26	51.0	0.05	9.2	0.20	39.2	0.38	0.72	12.5	116–102	101.6–100.6
13	905	1012			+	7.79	....	6.07	77.9	1.84	23.6	4.23	54.3	0.36	4.6	0.18	2.3	0.11	1.4	1.07	13.8	0.51	6.5	0.34	66.7	0.27	52.9	0.07	13.8	0.17	33.3	0.44	0.56	15.8	116–100	101.8–100.4
14	870	1014		0	+	8.34	....	6.38	76.5	5.58	66.9	0.60	7.2	0.37	4.4	0.10	1.2	0.09	1.0	1.41	17.1	0.56	6.7	0.35	62.5	0.32	53.6	0.05	7.9	0.21	37.5	0.63	0.51	14.8	116–100	101.4– 99.2
15	670	1018		0	+	5.89	....	4.35	73.2	1.54	26.1	3.01	50.9	0.28	4.8	0.03	0.6	0.05	0.9	0.98	16.5	0.40	6.7	0.27	67.5	0.24	60.0	0.03	7.5	0.13	32.5	0.40	0.40	13.2	110– 92	101.0– 99.8
16	820	1012				6.09	....	4.82	79.1	2.71	44.5	2.11	34.6	0.33	5.4	0.06	1.0	0.23	3.8	0.65	10.7	0.35	6.4	0.23	59.0	0.19	48.7	0.04	10.3	0.16	41.0	0.69	0.47	23.6	110–100	101.0– 99.8

Table 11.—Protein Metabolism in Case 11. Severe Pneumonia.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatinin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.						
2	845	1026	†	+	++	18.72	16.63	88.8	0.89	4.7	15.74	84.1	0.41	2.2	0.31	1.7	0.27	1.4	1.10	5.9	0.36	7.3	1.36	83.3	1.11	81.6	0.05	3.7	0.20	14.7	18.2	0.66	0.30	164–128	103.8–102.8
3	720	1027	†	+	++	19.20	17.54	91.4	1.02	5.3	16.52	86.1	0.33	1.7	0.07	0.4	0.30	1.5	0.56	5.0	1.27	6.6	1.11	87.4	1.05	82.7	0.06	4.7	0.16	12.6	16.7	0.66	0.04	112–104	103.0–101.2
4	800	1028	†	0	++++	22.51	20.82	92.5	1.48	6.6	19.34	85.9	0.38	1.7	0.11	0.5	0.34	1.5	0.86	3.8	1.44	6.9	1.32	91.7	1.24	86.2	0.08	5.5	0.12	8.3	14.0	0.87	0.00	100– 88	100.4– 98.8
5	620	1029	†	0	+++	16.39	15.21	92.8	0.86	5.3	14.35	87.5	0.30	1.9	0.09	0.6	0.24	1.5	0.55	3.3	1.06	6.5	0.94	88.7	0.88	83.0	0.06	5.7	0.12	11.3	21.8	0.73	0.15	96– 84	99.6– 98.4
6	730	1028	‡	0	+++	16.85	15.59	92.5	1.39	8.3	14.20	84.2	0.35	2.1	0.09	0.6	0.									Not determined.									92– 76	99.2– 98.6
7	840	1027	‡	0	+	17.87	16.07	89.9	1.53	8.6	14.54	81.3	0.43	2.5	0.08	0.4	0.									Not determined.									96– 72	101.2– 98.8
8	630	1029	†	0	++	15.33	11.94	89.5	0.74	5.5	11.20	84.0	0.32	2.4	0.11	0.8	0.19	1.4	0.77	5.9	0.84	6.3	0.74	88.1	0.71	84.5	0.03	3.6	0.10	11.9	13.0	0.98	1.89	86– 72	99.6– 98.4
9	1040	1025	†	0	.....	16.56	15.04	90.8	0.77	4.6	14.27	86.2	0.42	2.5	0.09	0.6	0.21	1.3	0.80	4.8	1.16	7.0	1.01	87.1	0.94	81.0	0.07	6.1	0.15	12.9	18.7	1.10	3.68	88– 76	99.2– 98.4
10	960	1020	†	0	0	13.67	12.50	91.4	0.75	5.5	11.75	85.9	0.36	2.7	0.07	0.5	0.17	1.3	0.57	4.1	1.00	7.3	0.86	86.0	0.81	81.0	0.05	5.0	0.14	14.0	24.3	1.12	2.07	88– 72	99.2– 98.4

and defervescence began and was completed on the morning of the 18th, on which day he was greatly improved. On the 19th and 20th, he was comfortable and convalescent; on the 21st, pleuritic pain was marked; on the 22d, patient was comfortable; on the 23d, he sat up in bed. On the 24th, he was up in ward, and on the 25th, discharged.

The urines in this case were examined during the period of the crisis, which had apparently begun before the examination. The maximum rise in nitrogen took place on the fourth day, when the temperature had practically reached normal. There was a slight increase also on the seventh day, accompanied, however, by a distinct but fleeting rise in the temperature. From then on the patient passed into a condition of practical nitrogen equilibrium.

The creatinin nitrogen was low. On the first day of the examination a notable quantity of creatin nitrogen was excreted, 0.31 gm., but this rapidly fell, and while throughout the examination small quantities were constantly present, the amounts excreted daily were small.

While the chlorin disappeared entirely, on one day of the examination, the phosphorus increased steadily, reaching its maximum on the last day of the disease. The chlorin had, however, become maximal in amount the day previous.

Case 12—The patient, H. C., male, 27 years of age, until one year ago was very alcoholic; had syphilis seven years ago; was admitted on sixth day of disease with left upper lobe involved and with a small area in the upper portion of the right lower lobe and also area in the right upper lobe. He seemed dull and sicker than his symptoms indicated. On the night of the 21st he was restless and uncomfortable; on the 22d, nauseated and vomited his food, was restless, dull, and seemed severely sick. New area of consolidation appeared in the right upper lobe. On the 23d, the patient was more comfortable and general condition improved; began to defervesce. On the 24th, defervescence was complete and general condition much improved. On the 25th, consolidation in left lower lobe was resolving, patient comfortable, and general condition excellent. On the 26th, patient was convalescent, and continued so uninterruptedly.

This case was one characterized clinically as very severely toxic in type, and a review of the results given by the examination of the urine substantiates that view.

The urine was examined from the time of entrance of the patient to the hospital. The defervescence extended over four days. On these days the nitrogen excretion varied between 31.2 and 27.2 gm. Even after a normal temperature was reached the nitrogen elimination still continued excessively high, and for five days (in one of which the urine was lost) the nitrogen excreted was from 22.7 to 18.3 gm. Not only is the total nitrogen output high, but during the febrile period the ratio of amid nitrogen to total nitrogen is much below the normal for this amount of nitrogen. As the ammonia ratio is low—quite within the supposedly normal limits for this amount of nitrogen—the rest nitrogen rises to most unusual absolute values.

On the first day of the examination unknown substances containing 5.82 gm. of nitrogen were excreted. In only one (Case 13) of the other cases have we found amounts in any way approaching this. For seven days a very high rest nitrogen was exhibited, falling at times to 1.01. On the fifteenth day of the disease the composition of the urine changed completely from that of the previous day. The patient went instantly into practical nitrogen balance and produced a urine normal in composition. The creatinin output on the first days of the examination was well above what has been found in the cases so far discussed, falling on the ninth day to a value to be found in most normal cases of this disease.

The creatin output is extremely high, on some of the days approaching very closely to creatinin output itself. It is noticeable also that the final fall in creatin precedes the day of low nitrogen excretion. Throughout the febrile period of the case the uric-acid nitrogen is also extremely high. Its fall precedes that of the total nitrogen.

With the exception of the first two days, one notes that the ratios obtained for the total sulphate sulphur to total sulphur are very high, so that as a consequence the neutral sulphur is comparatively low, especially when one compares it with the excessive amount of rest nitrogen excreted. One can only believe, therefore, that in this case in the group of unknown substances excreted as rest nitrogen there is a relatively great preponderance of those which contain a very low proportion of sulphur.

Fatal Cases.

The following cases terminated fatally, but do not comprise the complete results of all examined. In some of the instances the delirium was so great that we were unable to collect twenty-four-hour specimens of urine. In some cases the patients

entered the hospital in an alcoholic delirium and no satisfactory history or examination could be made.

Case 13—The patient, J. W., male, age unknown, alcoholic, with delirium tremens, was admitted with right lower lobe and right upper lobe involved. No history was obtainable. On admission, May 2, patient was evidently seriously ill and delirious; on May 3, general condition was fair; there were paroxysms of marked dyspnea; the patient was still evidently seriously ill. On May 4, condition was about same; May 5, patient's general condition not as good; pulse was worse. On May 6, patient was still delirious; condition fair; May 7, about same; May 8, further extension in right upper lobe; delirium more pronounced, patient evidently worse. On May 9, temperature was lower, but pulse and respirations much worse. On the 10th, most of the day patient seemed a little better, but in late afternoon grew worse. Entire right lower lobe was consolidated, patient evidently worse. On the 13th, patient continued delirious, and pulse was worse in character and faster in rate. Condition was very bad. On the 14th, patient died.

This typical case we were able to examine over an extensive period, during which the temperature never fell to normal. It is like the preceding in showing an amount of undetermined nitrogen on the first day of the examination above that of any so far recorded in the literature.

Creatinin was excreted in an unusually high amount, on the first day of the examination. The patient was a small man, weighing probably not more than 70 kilos. In this instance the creatin coefficient was undoubtedly at least 11.0, a value which has only so far been approached in typhoid fever (30), and by Hoogenhuyze and Verploegh (31) in muscular effort in which the metabolism is at a very high level.

What is quite remarkable is the absence of creatin in these urines until the last of the examination, when the creatin nitrogen steadily rises. During the time no creatin was found a large amount of muscle tissue was probably catabolized. This unusual state of affairs would tend to show that the breaking down of body protein alone, such as occurs in starvation, is not the only factor essential to the appearance of creatin in the urine. It is notable also that the amount of creatin steadily rises until death occurs—the amount excreted on the day before death is highest. If one may use the relative figures which were obtained for an incomplete specimen of urine on the last day, one may assume that both creatinin and creatin were higher on these days than on any preceding.

The total sulphur in this case merits some attention. In most of the other cases examined the ratio of total sulphur to total nitrogen varied between 6.0 and 7.5. In this case much higher ratios obtained, in one day being 9.8; except on the first day when 9.6 per cent. of total nitrogen was excreted as total sulphur, the highest values were obtained at the end. One might be led to infer that this catabolism of a protein high in sulphur toward the end of the disease was significant, for it has been seen in other conditions—notably delayed chloroform poisoning in animals—but such is not altogether the case, for in other lethal cases of pneumonia which we have examined the ratios are low toward the end.

In this, as in Case 12, the ratios for the various components of the sulphur partition are high, denoting a very efficient capacity for oxidizing the large amount of sulphur excreted.

Case 14—The patient, J. W., was admitted with right lower lobe only involved; no history obtainable. On admission, and on March 1, the patient's general condition was good; he seemed severely sick. On the 2d, the left lower lobe became involved and patient's condition became more serious. On the 3d, he was very ill, though his general condition was not alarming. On the 4th, his condition was not better. On the 5th, patient was worse; became delirious. On the 5th, the right lower lobe was resolving, but general condition was very bad. On the 7th, he died.

This case shows a somewhat different course in the nitrogen metabolism, as the amount of nitrogen excreted rose toward the end. In this case we have the pneumonic condition attended with a nephritis so intense that on the day on which the patient died 8.33 gm. of albumin nitrogen, equivalent to about 52.1 gm. of albumin, were excreted. The amount of albumin excreted varied between wide limits and was not progressive. The ammonia nitrogen in this case was high. On the last day of the illness 48.5 per cent. of the total nitrogen, excluding albumin nitrogen, was excreted in this form. It is possible that the urine on this date was decomposed, but it is doubtful. It is worth while noting that in two cases the day of death was accompanied by an alkaline urine in which a large part of the nitrogen was excreted in the form of ammonia.

The creatinin nitrogen in this case exceeds on an average anything which has been found in any previous case, and on the day of death reaches a maximum. With the

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Chlorin.	Phosphorus.	Pulse.	Temp. ° Fahr.
								Gm.	Gm.		
6	1420	1027	+	+ + +	+	20.4	8.4	0.35	2.00	120–108	104.2–102.8
7	1320	1024	+	+	0	19.8	17.5	0.32	1.46	120–108	103.4–101.5
8	1360	1022	+	+	0	18.2	17.4	0.49	1.40	104– 92	102.0–101.5
9	1220	1023	+	+	0	10.5	11.0	0.88	1.74	88– 84	99.5– 99.0
10	980	1026	+	+	+	12.2	11.1	1.07	1.61	92– 76	98.6– 98.0
11	1000	1029	+	+	0	12.1	15.1	3.40	1.33	84– 80	99.5– 98.4
	Urine lost.										
13	1020	1026	+	+	0	4.8	5.9	7.09	1.14	92– 68	98.6– 98.4
14	1012	1027	+	0	0	11.1	11.6	7.39	1.28	84– 76	99.8– 98.6
15	385	1029	+	+	0	17.5	25.6	2.23	....	84– 84	99.4– 98.6
16	600	1025	+	0	0	12.7	21.4	5.22	0.62	92– 80	99.0– 98.2

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						h.		Gm.	Gm.		
1	1716	1017	+	+ + +	+ +	4	16.4	6.7	1.46	0.00	128–110	104.0–102.8
2	1000	1019	+	+ +	+ +						
3	1260	1017	+	+ +	+ +						
4	825	1018	+	+ + +	+ +	0	20.8	28.0	0.22	0.15	132– 88	105.2–103.8
5	1360	1019	+	+ + +	+ +	1	19.7	36.2	0.35	0.15	152–100	105.4–102.6
6	1365	1020	+	+ +	+ +	3	17.3	27.0	0.94	0.08	136–118	104.8–104.0
7	1360	1019	+	+	+ + +	1	11.4	21.0	0.82	0.08	140–110	103.8–102.0
8	1040	1020	+	+	+ + +	5	8.6	15.0	1.22	0.24	140–128	104.8–102.6
9	1160	1024	+	+	+ + +	4	10.7	16.7	0.48	0.19	132–120	102.4–100.2
10	1220	1023	+	0	+ + +	1	7.1	11.6	1.05	0.28	144–120	105.0–100.8
11	780	1025	+	0	+ + +	4	8.6	11.3	1.32	0.00	144–112	104.4–100.8
12	940	1022	+	0	+ + +	0	7.9	10.9	1.19	0.05	140–120	103.6–100.2
13	....	1021	+	+	.....	3	9.9	16.7	0.99	0.11	140–120	104.0–101.0
						.	6.6	....	....	....	132–120	104.2–103.2

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Per Cent. T. S.	Chlorin.	Phosphorus.	Neutral S.: Rest Nitrogen.	Pulse.	Temp. ° Fahr.
							Gm.	Gm.			
3	975	1023	+	+ + +	0	33.9	1.60	1.50	48.2	124–106	105.2–101.2
4	1645	1019	+	+ + + +	+	7.6	2.99	0.98	8.4	138–120	105.2–102.0
5	1720	1012	+	+ + +	0	23.4	0.52	1.25	22.8	136–120	104.6–103.8
6	1620	1013	+	+ + +	0	17.9	0.88	1.02	13.2	136–120	104.0–103.0
7	1640	1027	+	+ + + +	+	31.0	0.70	....	42.3	130–112	105.0–104.0

TABLE 12.—PROTEIN METABOLISM IN CASE 12. SEVERE PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Albumin Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Chlorin.	Phosphorus.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			Gm.	Gm.		
6	1420	1027	†	+ + +	+	31.2	1.00	24.00	76.9	1.16	3.7	22.84	73.2	0.70	2.2	0.44	1.4	0.24	0.8	5.82	18.7	2.40	7.7	1.91	79.6	1.88	78.3	0.03	1.3	0.49	20.4	8.4	0.35	2.00	120–108	104.2–102.8
7	1320	1024	†	+	0	30.54	....	26.65	87.3	1.24	4.1	25.41	83.2	0.61	2.0	0.55	1.8	0.45	1.5	2.28	7.4	2.02	6.4	1.62	80.2	1.56	77.2	0.06	3.0	0.40	19.8	17.5	0.33	1.46	120–108	103.4–101.5
8	1360	1022	†	+	0	31.32	....	27.52	88.1	1.37	4.4	26.15	83.7	0.60	1.9	0.49	1.6	0.49	1.6	2.12	6.8	2.03	6.4	1.66	81.8	1.61	79.3	0.05	2.5	0.37	18.2	17.4	0.49	1.40	104– 92	102.6–101.5
9	1230	1023	†	+	0	27.20	....	24.55	90.3	1.05	3.9	23.55	86.4	0.42	1.6	0.30	1.1	0.30	1.1	1.63	5.9	1.71	6.9	1.53	89.5	1.48	86.6	0.05	2.9	0.18	10.5	11.0	0.88	1.74	88– 84	99.5– 99.0
10	980	1026	†	+	+	22.72	....	20.02	90.1	0.51	2.2	19.51	87.9	0.46	2.0	0.17	0.7	0.36	1.4	1.71	5.8	1.56	6.8	1.37	87.8	1.30	83.3	0.07	4.5	0.19	12.2	13.1	1.07	1.61	92– 76	98.6– 98.0
11	1000	1029	†	+	0	22.53	....	20.48	90.9	0.93	4.1	19.55	86.8	0.41	1.8	0.20	0.9	0.18	0.8	1.26	5.6	1.58	7.0	1.39	87.9	1.32	84.1	0.07	3.8	0.19	12.1	15.1	3.40	1.33	84– 80	99.5– 98.4
	Urine lost.																																		
13	1020	1026	†	+	0	18.32	....	16.69	90.1	1.04	5.7	15.65	85.4	0.42	2.3	0.11	0.6	0.09	0.5	1.01	5.5	1.25	6.8	1.19	995.2	1.13	90.4	0.06	4.8	0.06	4.8	5.9	7.09	1.14	92– 68	98.6– 98.4
14	1012	1027	†	0	0	19.24	....	17.23	89.5	1.21	6.3	16.02	83.2	0.50	2.6	0.05	0.3	0.17	0.9	1.29	6.7	1.35	7.0	1.20	88.9	1.15	85.2	0.05	3.7	0.15	11.1	11.6	7.39	1.28	84– 76	99.6– 98.6
15	385	1029	†	0	0	8.09	....	7.41	91.5	0.50	6.1	6.91	85.4	0.18	2.2	0.04	0.5	0.07	0.9	0.39	4.9	0.57	7.0	0.47	82.5	0.43	75.4	0.04	7.1	0.10	17.5	25.6	2.23	....	84– 84	99.4– 98.6
16	690	1025	†	0	0	9.78	....	9.00	92.0	0.72	7.4	8.28	84.6	0.25	2.6	0.03	0.3	0.08	0.8	0.42	4.3	0.71	7.2	0.62	87.3	0.57	80.3	0.05	7.0	0.09	12.7	21.4	5.22	0.62	92– 80	99.0– 98.2

TABLE 13.—PROTEIN METABOLISM IN CASE 13. FATAL PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Albumin Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Phosphorus.	Chlorin.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			Gm.	Gm.		
1	1716	1017	†	+ + +	+ +	27.85	0.53	19.65	72.0	1.63	6.0	18.02	66.0	0.79	2.9	0.00	0.0	0.31	1.1	6.57	24.0	2.68	9.6	2.24	83.6	2.19	87.6	0.05	2.0	0.44	16.4	6.7	1.46	0.00	128–110	104.0–102.8
2	1000	1019	‡	+ +	+ +	Urine decomposed.																														
3	1260	1017	‡	+	+ +	21.62	....	19.47	90.1	1.40	6.5	18.07	83.6	0.58	2.7	0.00	0.0	0.14	0.7	1.43	6.5	1.93	8.9	1.53	79.2	1.48	76.5	0.05	2.7	0.40	20.8	28.0	0.22	0.15	132– 68	105.2–103.8
4	825	1018	†	+ + +	+ +	15.25	0.10	14.15	93.4	0.45	3.0	13.70	90.4	0.35	2.3	0.00	0.0	0.07	0.5	0.58	3.8	1.07	7.0	0.86	80.3	0.82	76.6	0.04	3.7	0.21	19.7	36.2	0.35	0.15	152–100	105.4–102.6
5	1360	1019	†	+ +	+ +	23.88	0.28	21.50	91.2	0.61	2.6	20.89	88.6	0.64	2.7	0.00	0.0	0.24	1.0	1.22	5.1	1.91	8.0	1.58	82.7	1.51	79.1	0.07	3.6	0.33	17.3	27.0	0.94	0.08	136–118	104.8–104.0
6	1365	1020	†	+ +	+ +	26.28	....	24.50	93.4	1.43	5.5	23.07	87.9	0.57	2.2	0.00	0.0	0.17	0.8	1.01	3.6	1.84	7.0	1.62	88.6	1.56	84.8	0.07	3.8	0.21	11.4	21.0	0.82	0.08	140–110	103.8–102.0
7	1360	1019	†	+	+ + +	28.90	....	27.26	94.4	0.54	1.9	26.72	92.5	0.47	1.6	0.09	0.3	0.07	0.2	1.01	3.5	1.75	6.1	1.60	91.4	1.50	85.7	0.10	5.7	0.15	8.6	15.0	1.22	0.24	140–128	104.8–102.6
8	1040	1020	†	+	+ + +	24.17	....	22.70	94.0	1.90	7.8	20.80	86.2	0.38	1.5	0.04	0.2	0.21	0.8	0.84	3.5	1.31	5.5	1.17	89.3	1.09	83.2	0.08	6.1	0.14	10.7	16.7	0.48	0.19	132–120	102.4–102.2
9	1160	1024	†	+	+ + +	25.46	....	23.76	93.3	0.41	1.6	23.35	91.7	0.56	2.2	0.06	0.2	0.13	0.5	0.95	3.8	1.54	6.0	1.43	92.9	1.35	87.7	0.08	5.2	0.11	7.1	11.6	1.05	0.28	144–120	105.0–100.8
10	1220	1023	†	0	+ + + +	26.47	....	24.50	92.5	0.30	1.1	24.20	91.4	0.51	1.9	0.08	0.3	0.14	0.5	1.24	4.8	1.62	6.1	1.48	91.4	1.40	86.4	0.08	5.0	0.14	8.6	11.3	1.32	0.00	144–112	104.4–100.8
11	780	1025	†	0	+ + + +	12.78	....	11.22	88.0	0.30	2.3	10.92	85.5	0.40	3.1	0.03	1.0	0.08	0.6	0.92	7.3	1.36	9.8	1.16	92.1	1.07	84.9	0.09	7.2	0.10	7.9	10.9	1.19	0.05	140–120	103.6–100.2
12	940	1022	†	0	+ + + +	14.23	....	12.73	89.4	0.23	1.6	12.50	87.8	0.38	2.6	0.26	1.8	0.08	0.6	0.78	5.4	1.16	9.2	1.04	90.1	1.04	79.4	0.14	10.7	0.13	9.9	16.7	0.99	0.11	140–120	104.0–101.0
13	....	1021	†	+	....	....	....	....	83.5	....	3.8	....	79.7	....	....	5.1	....	2.7	....	....	....	....	....	....	93.4	....	87.6	....	5.8	....	6.6	....	....	....	....	132–120	104.2–103.2

TABLE 14.—PROTEIN METABOLISM IN CASE 14. FATAL PNEUMONIA.

Day of Disease.	Volume c.c.	Specific Gravity.	Reaction.	Albumin.	Indican.	Total Nitrogen.	Albumin Nitrogen.	Amid Nitrogen.	Per Cent. T. N.	Ammonia Nitrogen.	Per Cent. T. N.	Urea Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Creatin Nitrogen.	Per Cent. T. N.	Uric Acid Nitrogen.	Per Cent. T. N.	Rest Nitrogen.	Per Cent. T. N.	Total Sulphur.	T. S.: T. N.	Total Sulphate Sulphur.	Per Cent. T. S.	Alkali Sulphate Sulphur.	Per Cent. T. S.	Ethereal Sulphate Sulphur.	Per Cent. T. S.	Neutral Sulphur.	Per Cent. T. S.	Neutral S.: Rest Nitrogen.	Chlorin.	Phosphorus.	Pulse.	Temp. ° Fahr.
						Gm.	Gm.	Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.		Gm.			Gm.	Gm.		
3	975	1023	†	+ + +	0	16.48	2.81	11.76	86.3	1.14	8.4	10.64	77.9	0.74	5.4	0.00	0.0	0.28	1.7	0.85	6.6	1.21	7.3	0.80	66.1	0.77	63.6	0.03	2.5	0.41	33.9	1.60	1.50	48.2	124–106	105.2–101.2
4	1645	1019	†	+ + + +	+	27.80	6.76	18.00	85.6	1.00	4.7	17.00	80.9	0.72	3.4	0.56	2.6	0.34	1.6	1.42	6.8	1.57	5.6	1.45	92.4	1.42	90.5	0.03	1.9	0.12	7.6	2.99	0.98	8.4	138–120	105.2–103.0
5	1720	1012	†	+ + +	0	19.10	1.44	15.12	85.6	1.74	9.8	13.38	75.8	0.66	3.4	0.41	2.5	0.24	1.4	1.27	7.2	1.24	6.5	0.95	76.6	0.92	74.2	0.03	2.4	0.29	23.4	0.52	1.25	22.8	136–120	104.6–103.8
6	1620	1013	†	+ + +	0	21.02	2.38	15.36	82.4	1.18	6.3	14.18	76.1	0.62	3.3	0.58	3.1	0.19	1.0	1.89	10.2	1.39	6.6	1.14	82.1	1.12	80.6	0.02	1.5	0.25	17.9	0.88	1.02	11.2	136–120	104.0–103.0
7	1640	1027	‡	+ + + +	+	29.14	8.33	17.40	83.6	10.10	48.5	7.30	35.1	0.75	3.6	0.64	3.1	0.43	2.5	1.58	7.2	2.16	7.4	1.49	69.0	1.44	66.7	0.05	2.3	0.67	31.0	0.70	....	42.3	136–112	103.6–104.0

high output of creatin we have a most unusually high creatin elimination, suddenly appearing on the second day of the examination. Clinically the case might easily be compared with the preceding, yet there is a marked difference in the metabolism of the two cases. In the one no creatin is found; in the other, creatin appears in the urine and reaches a level which is not found in any of the other cases examined.

The uric acid nitrogen is high throughout, but does not call for any special comment, except to point out the unusual amount, 0.43 gm., excreted on the terminal day.

The rest nitrogen, compared with what has been found in some of the other cases of severe toxic pneumonia, is both relatively and absolutely low.

A comparison of the neutral sulphur with the undetermined nitrogen shows the fluctuating character of the latter, with respect to sulphur. The ratios vary from 48.2 to as low as 8.4. No relationship with the severity of the condition nor with any of the important factors of the nitrogen partition can be made out.

Summary.

The nitrogen and sulphur metabolism in 19 cases of pneumonia of varying degrees of severity have been examined.

The cases of milder type show a smaller loss in nitrogen and sulphur than do those of a more severe grade. The daily loss in nitrogen on a diet adequate to protect a resting individual from nitrogen loss may be from 20 to 25 gm.

The relative desamidating capacity, as shown by the ratio of urea nitrogen to total nitrogen, is comparable to that of a normal subject. The capacity for the oxidation of the cystin group, as exhibited by the ratio of total sulphate sulphur to total sulphur, is quite as high, if not higher than normal.

During the period of hyperpyrexia excessive amounts of creatinin are elminated. This is followed during convalescence by a subnormal excretion of creatinin. This is taken to indicate the endeavor on the part of the organism to repair the losses sustained during the height of the toxemia.

In the severe cases of pneumonia large amounts of creatin are also excreted. This is seen particularly during the time of greatest nitrogen loss. During convalescence the creatin disappears from the urine. In some of the lethal cases the amount of creatin excreted on the day terminating the illness is as high as the amount of creatinin excreted.

During hyperpyrexia, especially in cases severely toxic in type, unusually high amounts of undetermined nitrogen are excreted. In some cases over 5 gm. of nitrogen derived from uninvestigated substances are found in the urine. This nitrogen is not derived from albumoses, as the search for these substances revealed quantities which in no way could account for the large amount of rest nitrogen.

The sulphur excretion runs more or less parallel with that of the nitrogen; but it appears in some of the cases that the catabolism of proteins rich in sulphur is not so marked as those in which the control of sulphur is small. On the other hand, cases progressing unfavorably seem to show an excessive destruction of proteins containing much sulphur. This is made out from the increased ratio of total sulphur to total nitrogen.

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28. The malted starch was made by taking arrowroot starch, heating with water in a double boiler, and after cooling to 70 C. allowing an extract of malt to act on the starch in order to effect a partial conversion into maltose. The resulting mixture of maltose and starch is fluid while hot and semi-solid when cold. When flavored with lemon or vanilla it is readily taken by patient.
29. It will be instructive to note the explanation of this high creatin output in cases of typhoid which has been offered by Ewing and Wolf (The Archives Int. Med., 1909, iv, 336). A similar explanation will satisfy the difference which one observes in the total nitrogen and creatin output in Cases 3 and 7 of this series.
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A CASE OF TETANUS, WITH POINT OF INFECTION THE CAVITY OF A TOOTH.

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Tetanus has been reported following injuries to nearly every part of the human body. The wound may be so insignificant and microsopic that its presence is either forgotten or not known. Minute scratches, slight abrasions of skin, leech-bite and bee stings, prick of needle, even hypodermic needles have been reported as the wounds of entrance of the tetanus bacillus. The following case is reported, because a search of medical literature does not reveal its analogue, because of the importance of knowing that it is possible to have tetanus enter the body through a cavity in a tooth and emphasizing the necessity of the care of such teeth, calling attention to the dangers of picking, with indiscriminate implements, the teeth, and lastly because we have here an opportunity, with the assistance of a very excellent bacteriological examination, to diagnose properly a positive case of tetanus in which there is no external visible wound on the body save the cavity of a tooth.

M. H., 10 years of age, admitted to my service at the Harlem Hospital on February 22, 1905. Referred by Dr. Loucks. Family history; both parents living and well, no diathesis traceable. Previous history; had measles as an infant, no other illness, but has a tendency toward indigestion, has had slight growing pains. Is a nervous child, somewhat emotional, subject to toothache, and has a habit of picking the teeth with anything that comes to hand—a straw, needle, or a pin.

Present Illness—Began four days ago with slight swelling of the neck, which was a little stiff. She was able, however, to talk and eat. The next morning she could open her mouth but a very little, and by evening the trismus was pronounced. She complains of headache and soreness of her teeth. She has not had any tonic or clonic convulsions of any part of her body. Her whole body is slightly spastic, but not sufficient to interfere with the patella reflex, which is very brisk and markedly exaggerated. She has had no food and but little sleep during this time, and is an object of distress, as her buccal secretions constantly dribble from the angles of her mouth. No history of any punctured wound is obtainable, the only trauma received lately being a blow on the vertex with a stick, which, however, the parent claims, left no mark.

Present Condition—Conscious, rational, fairly well developed and nourished; general convulsive movements. Eyes: increased secretions, slight nystagmus, ocular excursion fair, pupils equal, semidilated and reacting. Mucous membranes of fair color. Tongue: moist, slightly coated. Mouth: several carious teeth on lower jaw, profuse salivation, and considerable foaming at mouth; pharynx not examined as jaws could not be sufficiently opened to admit of it. Heart: normal size and position, rapid and regular; no adventitious sounds. Arteries: normal, Pulse: full, moderate force, slight tension, rapid and regular. Lungs: normal chest, poor expansion, moderate respirations, slight dyspnea, fair fremitus and resonant note. Normal voice and breathing sounds; no adventitious sounds. Abdomen: slightly retracted, board-like rigidity, no mass nor tenderness, tympanitic note. Liver, Spleen and Kidneys: normal. Skin: smooth, soft, fair color, dry and warm; no rash nor eruption. Bones and Joints: apparently no organic lesions, marked rigidity of jaws and spasticity of most joints. Muscles: tonic contracture of muscles of jaw and abdomen: irritability of most of other muscles. Lymph nodes: quite large submaxillary. Reflexes: exaggerated.

February 22: Patient very restless, vomited once during the day; clear fluid. Takes a little fluid by mouth, but no solids; jaws quite rigid, mouth closed, con-

siderable salivation, abdomen remarkably rigid and board-like. 10 P. M.: Very restless this evening. Apparently unable to swallow, so put on nutritive enemata. February 23, A. M.: Had numerous clonic seizures during the night and one slight tonic convulsion about 1 A. M.; retained nutritive enemata fairly well, salivation very profuse. Had three severe convulsions about 10 A. M.

March 1: Taken to operating room, and three teeth (two bicuspids and a canine) removed. Jaws were so rigid that anesthetic was attempted, but patient immediately had a seizure which was very severe. Amyl nitrite was used to overcome it, and slowly quieted her, clearing up the marked cyanosis, but was followed in quick succession by three more convulsions, while on operating table. This being clearly a case of head tetanus, it had been our intentions to trephine and do a subdural injection, but the patient's condition, rapidly getting worse, precluded this, and we had to be content with a spinal puncture. About 22 c.c. of spinal fluid were withdrawn and 18 c.c. of tetanus antitoxin injected. The cavities caused by extracting teeth were swabbed out with tincture of iodine. Mouth washed with boric acid and myrrh solution, nourishment given per tube in mouth. Patient has had severe clonic contractions during the day, but was conscious mostly all of the time and apparently rational. After a severe spasm about 6 P. M., patient was very weak, breathing became stertorous and pulse imperceptible at wrist. She was carried along for nearly an hour by stimulation, when she had another tonic seizure, during which she died. During tonic spasm jaws became very hard set, abdomen distinctly board-like, rigidity considerable, marked opisthotonos, profuse salivation; then legs became rigid, and lastly arms. Breathing practically ceased, face became livid, and mucous membranes purple.

Urine: February 22, pale yellow, opaque, heavy, muddy sediment acid. Specific gravity, 1037; slight quantity of albumin present. Sugar negative. Amorphous urates, Leucocytes, and epithelial cylindroids present.

A diagnosis of tetanus having been made from the clinical picture, as there was no other visible wound on the body save the carious teeth, they were removed and placed in a sterilized container and submitted for examination to Dr. Leo Buerger, who reports the following: The material for examination consisted of two foul-smelling, dirty, necrotic teeth, the larger portion of a third tooth, together with a small, ragged tooth fragment. Spreads made from many parts of this material showed a multiplicity of bacteria, none of which could be identified as tetanus bacilli in the stained specimen. There were streptococci, staphylococci, Gram negative and Gram positive bacilli of the most diverse morphology, spirilla, and diplococci.

The bacteriological examination of the material was conducted as follows: First, by direct animal inoculation, and, secondly, by culture.

Animal Inoculations—A guinea pig, weighing 300 gm. received 0.5 c.c of a saline suspension (made by shaking up all the material in 2 c.c. of sterile normal salt solution) subcutaneously in the right groin. The small, ragged fragment of tooth, above mentioned, was also inserted in a small pocket, under the skin, made a short distance above the point of inoculation. On the seventh day the right leg became spastic. On the eighth an occasional general body tremor could be observed. The spasticity of the limb was more marked, and the animal quite sick. The stiffness of the limb persisted for four more days. There was suppuration at the site of inoculation, but the guinea pig recovered. Three weeks after the inoculation the wound was completely healed. White mouse No. 1 received 0.25 c.c. of the same suspension, subcutaneously in the right groin. No observation having been made during the nine to twelve hours before death, any tetanic symptoms which may have occurred during that period were not recorded. However, the animal died in seventy-two hours, the body being found markedly bent upon itself, an evidence apparently of convulsions before death. The autopsy on this mouse showed a foul-smelling abscess in the right groin. Spreads made from the pus of this abscess did not demonstrate the presence of any tetanus bacilli. Two loopfuls of this pus were emulsified in sterile salt solution and injected under the skin of right groin of another white mouse (No. 2). Mouse No. 2: Inoculated February 26, at 5 P. M., with the above-mentioned pus. On February 27, A. M., right leg spastic and extended. 2 P. M., right fore limb also spastic, with some rigidity of the whole right side of the body. 5 P. M., left side of the body becoming involved, first some rigidity of left hind limb; later of the left fore limb. 8 P. M., general convulsions. 10 P. M., killed by means of chloroform. Autopsy showed no macroscopic lesion.

Culture Experiments—A pure culture of typical tetanus bacilli was isolated from the emulsion made by washing all the material in sterile normal salt solution. The methods of Kitasato were employed. The pathogenicity of the organism was determined in the following animal experiments:

White mouse No. 1 received 0.2 c.c. of a two days' culture of the tetanus bacilli in neutral broth at 10:30 A. M., February 28, 1905. The injection was made under the skin on the right groin. After eleven and a half hours the right hind limb became spastic. Then there followed a gradual involvement of the other extremities, with general convulsions and death in twenty-one and a half hours. Guinea pig No. 1, weighing 300 gm., received 0.25 of the same culture under the skin of the right groin. Death occurred in twenty-three and three-fourths hours. It was preceded first by stiffness of the right hind leg, then general extension of the spasticity, and finally convulsive movements.

Guinea pig No. 2, weighing 600 gm., received four loops of the same culture in the same region. The period of inoculation was two days. Then the typical symptoms set in, and death ensued at the end of three days and eleven hours. Mouse No. 2, injected in the same situation with one loop of the culture, died of tetanus in thirty-nine hours. By this work we have removed a positive case of tetanus from where it otherwise would have been assigned, *i. e.* the broad, questionable field of so-called tetanus idiopathicus, and proven that it is possible to have an infection of the *Bacillus tetani* enter the human body through a cavity in a tooth.

ORIGINAL COMMUNICATION.

TETANUS CURED WITH ANTITOXIN.

W. Gilman Thompson, M.D.

The following case, not heretofore published, illustrates in striking manner the curative effect of tetanus antitoxin. The patient, a man 36 years of age, while employed as a laborer in tearing down an old building, stepped upon a rusty iron nail which penetrated his shoe and cut the sole of the right foot immediately behind the third toe. Eleven days later the patient first noticed that his legs were becoming very stiff, and the following day he could open his mouth only with considerable difficulty. The stiffness of his muscles rapidly became generalized, and on the fourteenth day after the injury he was brought into the hospital in complete opisthotonos. The abdomen was board-like, the teeth were tightly clenched, there was a risus sardonicus and the extremities were so rigid that the patient might have been lifted horizontally from the bed by one leg. He complained of no pain, but there were slight muscular twitchings. Slight albuminuria was present with a few hyaline and granular casts. While in hospital he presented a very irregular septic type of temperature, both intermittent and remittent, which lasted in all sixteen days. The maximum elevation was at 105° F., with two records of 104° F. The pulse ranged from 70 to 140. There was a high degree of leucocytosis, the maximum count yielding 52,000 white corpuscles with a polynucleosis of 96.2 per cent. The patient was fed by rectum and by dropping fluid nourishment between the clenched teeth. His condition was extremely critical, and for the first forty-eight hours recovery did not seem possible.

The wound in the foot was re-opened and cauterized with iodine, and the patient was immediately given 3,000 tetanus antitoxin units furnished by the laboratories of the Department of Health. This dose was repeated three times on succeeding days when the rigidity gradually lessened and the patient showed marked improvement in other ways, the temperature temporarily falling to normal. As it did not remain normal, however, three succeeding doses of 1,500 units were given. Further improvement followed so that after seven or eight days the patient was able to move the arms and legs with some freedom. Several smaller doses (750 units) were then given, and by the fourteenth day after the first dose, the patient was able to stand. A day or two later the temperature again rose to 102° F., but was controlled by a single dose of 3,000 units, after which the patient was able to walk and had no further trouble. In all the patient received eleven injections, all, with one exception, being intravenous, in the veins of the arms and legs. The exception was a single dose given subcutaneously. The total number of units administered was 22,500. This case illustrates well the septic type of the disease, with wide temperature excursions, tendency to relapse, a high leucocytosis and high polynucleosis. It also emphasizes the value of prompt and persistent intravenous injections of antitoxin.

FOUR CASES OF ACUTE HEMORRHAGIC PANCREATITIS, ASSOCIATED WITH FAT NECROSIS.*

B. C. Crowell, M.D.

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Since Fitz in 1889 described the condition of acute hemorrhagic pancreatitis, an abundant literature on the subject has accumulated, and much excellent experimental work has been reported, the latter having been an attempt to clear up the etiology of the condition. However, the number of cases in human beings which come to autopsy is not as yet so great as to preclude their presentation, in the hope of at least furnishing further data for future investigators.

The chief problems to be solved in this condition seem to be related to the etiology, and numerous theories have been evolved to explain the manner in which the condition arises. The series of cases which I am to present demonstrates that Opie's theory of obstruction at the duodenal orifice of the common bile duct by calculi and the passage of bile into the duct of Wirsung cannot explain all cases. Another hypothesis is that of Thiroloix, who notices the frequent association of cholelithiasis and claims a common bacterial cause for gall-stones and acute pancreatitis, the pancreatic lesion being set up, according to this author, by lymphatic transmission of bacteria from gall-bladder to pancreas. The evidence produced to uphold this doctrine seems somewhat open to question. Other possibilities are infections traveling down the bile ducts and up into the pancreas, or from duodenum to pancreas. That intestinal contents can be forced up into the pancreas only with the greatest difficulty has been demonstrated in the dog, and Pearce's report of a case of gastro-pancreatic fistula without acute pancreatitis seems to demonstrate that gastric juice alone will not cause the lesion. The production of fat necrosis has been proven experimentally by Flexner, Opie, and others to be due to the action of the fat splitting ferment of the pancreas. As Wells has pointed out, this fat necrosis differs from simple necrosis in sharp limitation of the affected area, by a wall of leucocytes and later of connective tissue, and by the filling of the necrosed cells by the products of fat splitting, lime salts being frequently deposited in the necrotic areas in the process of healing. It is interesting to note that this process in no way differs from that which Klotz has described as occurring in sclerosing vessels.

The first case presents in brief the following features: Three days previous to death the patient had sudden abdominal pain and distention, with rigidity. There was slight fever, and the pulse rate varied from 90 to 120. He was operated on, and the diagnosis made. At autopsy he was found to be a large, well-nourished male of 29 years of age. There was no free fluid in the abdomen and no peritoneal adhesions were present. The omentum was large and fatty, but without evidence of fat necrosis. The heart, kidneys and liver were the seat of acute parenchymatous degeneration. In the liver there were also numerous subcapular hemorrhages and the congested lungs were the seat of a bronchopneumonia. The alimentary tract and other viscera, except those to be described, were normal. Fat necrosis was seen in the pancreas, and peripancreatic, periportal, and perirenal fat. Hemorrhagic infiltration was present in the peripancreatic and perirenal tissues.

The pancreas was enlarged, especially in its head and body. The head was enlarged, brownish, soft and greasy. The body was firm, pink, and fleshy in appearance, while the tail showed extensive hemorrhagic infiltration and fat necrosis. The interlobular septa were thickened, greyish, and necrotic in appearance. The pancreatic duct was of normal caliber, contained brownish yellow fluid, and opened in the ampulla separately from the common bile duct. The gall-bladder was distended and contained dark, tarry bile. The cystic, hepatic, and common ducts were of normal caliber and appearance, no calculi being anywhere present. The mucosa of the duodenum was bile stained and the mesenteric lymph-nodes small and pale.

The second case was one of an obese male of 48 years of age, who was found to have extensive arteriosclerosis, fibroid myocarditis, congested lungs, fatty liver, and normal kidneys and gastro-intestinal tract. There was no free fluid in the abdomen. Numerous foci of fat necrosis were found in the mesocolic, omental, peripancreatic and peritoneal fat. The pancreas was enlarged and the seat of

* From the Proceedings of the New York Pathological Society, February and March, 1909.

necrosis and hemorrhagic infiltration. The pancreatic duct was patent and of normal caliber, as were also the cystic, hepatic, and common bile ducts. The gall-bladder contained one calculus, 15 mm. in diameter, adherent to its fundus, and some bile. There was no apparent obstruction to the outflow of either bile or pancreatic secretion, no dilatation of the ducts, and no evidence of a calculus having passed through them; nor was a calculus found in the intestine.

The third case was that of a very obese male of 60 years of age, who clinically presented the symptoms of sudden severe abdominal pain and distention, icterus, ileus, collapse, glycosuria and death in thirty-six hours from the onset of pain. At autopsy the obesity and jaundice were remarkable. The heart showed slight hypertrophy, and some early sclerosis of the coronary arteries and aorta. The lungs were emphysematous and congested, with a few synechiæ at the right apex, and one peritracheal node was calcified. The spleen was atrophic, and the splenic and superior mesenteric veins were the seat of recent thrombi, the portal vein being free. The liver and kidneys were the seat of acute parenchymatous degeneration. There was a considerable distention of the abdomen by a large amount of hemorrhagic fluid, in which oil droplets were visible.

The extent of the areas of fat necrosis was most remarkable. These areas were present in the parietal subperitoneal fat, in the omentum, perirenal fat, the peripancreatic fat, the pancreas, and the appendices epiploicæ in enormous numbers, varying in size up to a diameter of 4 mm. They were circular, definitely circumscribed, yellowish white to white in color, and pasty; and some were surrounded by a definite narrow circumscribing hyperemic zone. There was a considerable hemorrhagic infiltration of the abundant peripancreatic and perirenal fat.

The pancreas was enlarged to nearly three times its normal size, and its surface was reddish and brown in color, showing considerable hemorrhage. Section of the gland showed it to be of reddish brown color, with extensive hemorrhagic infiltration, and marked softening throughout, except for a small area in the middle part of the head of the gland where the normal appearance was preserved. Areas of fat necrosis were distributed irregularly throughout the gland. Dissection of the duct of Wirsung showed it to be somewhat distended, opening into the papilla of Vater 7 mm. from its apex, its mucosa not pigmented. Impacted in the ampulla was a gall-stone 7 mm. by 5mm., yellow and firm; and another smaller, soft, black pigment mass about 5 mm. long. The opening of the duct into the duodenum readily admitted a 2 mm. probe, the ampulla being 18 mm. in circumference, a considerable dilatation. The common, cystic, and hepatic ducts were dilated, but contained no other calculi except for one within the liver. The gall-bladder at its fundus was adherent to the liver, and was found to contain numerous gall-stones, the largest being spherical and 3 cm. in diameter. On section it was found to have a cholesterin center and cultures from it were sterile. Smaller pigment masses were also present and a very small amount of greenish turbid bile. The mucosa of the duodenum was bile-stained, and about 2 cm. above the opening of the papilla was found a small teat-like mass with central umbilication which was suspected to be the opening of the duct of Santorini, but on section this proved not to be so.

The last case was of a woman of 30 years of age, who was admitted to the hospital markedly alcoholic, with the history of six weeks' illness at home with little or no attendance, during which time she had consumed enormous quantities of whisky. On admission she was without fever, with feeble rapid pulse, cyanosis and marked prostration. Soon after admission she went into profound shock, had marked abdominal distention, and constipation, and died forty hours after admission. At autopsy, performed by courtesy of Drs. O'Hanlon and Larkin, she was found to be a woman of small frame, and very poor nutrition, without evidence of icterus. There was no free fluid in the abdomen. Numerous typical areas of fat necrosis were found in the sub-peritoneal fat anteriorly, in the omentum, in the pelvis over the bladder, in the perirenal fat, in the peripancreatic tissues and in the pancreas. In the thorax these areas were also present in large numbers in the tissues of the anterior mediastinum, and completely covered the parietal pleurae, being most marked on the left side. In the left pleural sac was a large amount of red clotted blood, and clear serous fluid. The lungs showed some congestion of the lower lobes, the heart a marked brown atrophy, the liver fatty infiltration, the kidneys acute parenchymatous degeneration; the spleen was normal and the vagina was the seat of slight ulceration. There were no venous thromboses. The duodenum contained some bile-stained mucus and considerable pressure on the gall-bladder was necessary to force bile through the papilla. On dissection all the bileducts were found normal in caliber and appearance, and no concretions were anywhere present. The gall-bladder contained a considerable amount of dark bile, with some mucus.

The pancreatic duct opened into the papilla beside the common duct, just within the duodenal orfice, so that the common duct and duct of Wirsung could not be converted into one channel by any mass in the papilla. The duct of Santorini was not found. The pancreas itself was enlarged to about twice its normal size and was distinctly firm; and numerous red patches were distributed over its surface, with a few small areas of fat necrosis between the lobules. On section it was of good consistence, the pancreatic tissue being pale, yellowish, firm, with fairly numerous areas of fat necrosis distributed throughout the interlobular tissue, and hemorrhagic areas which were of variable size, particularly numerous about the periphery of the gland.

Thus we have four cases, two which are associated with cholelithiasis, one of these fulfilling Opie's requirements. Three of them occurred in obese males between the ages of twenty-nine and sixty. The clinical features are remarkably similar, consisting essentially in sudden pain and distention of the abdomen, collapse, symptoms of ileus, coma, and death. If gall-stones are present, icterus may be marked. In the fourth case, with a history of prolonged illness, the fat necrosis had extended into the thorax, probably by lymphatic transmission.

In all, the histology is similar, consisting essentially of widespread necrosis of the gland, involving parenchyma and interstitial tissue, inflammatory exudate, serum and leucocytes and extensive hemorrhages. This hemorrhage infiltration takes place not only in the pancreas, but in far distant parts as the perirenal fat, and in one case the pleura.

A REPORT UPON THE VALUE OF NOGUCHI'S REACTION ON SPINAL FLUIDS.*

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The following report on the Noguchi reaction covers observations made in a series of thirty-one cases. We shall make no attempt to consider the subject from the viewpoint of the physiological chemist, but shall content ourselves with a short résumé covering simply the result of the test in each case with reference to the clinical or post-mortem findings.

For purposes of analysis we may group our material as follows:

Class I.—Test on cases during life and uncontrolled by autopsy.

Class II.—Tests on cases during life which were afterward controlled by autopsy.

Class III.—Tests on spinal fluids obtained at autopsy.

The technique employed was that described by Noguchi. (†)

Class I, of cases in which the spinal fluid was tested ante-mortem only, contained eighteen cases. As no autopsy was made in any of these, a fair margin of error must be allowed for. While there is generally little difficulty in determining the presence or absence of lues in young infants by the clinical evidences, in adults we are often on less certain ground in excluding syphilitic infections.

We shall, for present purposes, have to consider as non-syphilitic those cases in which syphilis is denied and the accepted clinical signs are absent, and include as probably non-syphilitic, cases in which the history is unobtainable or unreliable, and which show no clinical evidences of syphilis.

Let us first consider those cases known to be actively syphilitic. Of these there were but two, a tertiary syphilitic 27 years of age, who had had but two months' treatment following his initial lesion, and a case of congenital syphilis in an infant. In the first there was neither opalescence nor precipitate visible after standing con-

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* Reprinted from the Proceedings of the N. Y. Path. Soc., February and March, 1909.

† Journal of Experimental Medicine, 1909, xi, p. 84.

siderably over the required time, and the test was therefore negative. The second, which also gave a negative Noguchi, gave a positive Wassermann reaction.

Of the non-syphilitic cases, eleven in number, two were cases of lobar pneumonia and one of these was complicated by alcoholic cerebral edema. Both gave negative Noguchi reactions. A Wassermann tried on the uncomplicated case mentioned above was also negative. A case of bronchopneumonia with chronic alcoholism gave a negative Noguchi. A fourth case, a sacral abscess, gave a negative Noguchi and a negative Wassermann. Six cases of tuberculosis meningitis in patients of varying ages all gave positive Noguchi reactions. On one of these there was a negative Wassermann. A case of pneumococcus meningitis in a child of six months gave a positive Noguchi.

This series of positive reactions in seven consecutive cases of meningitis seems worthy of attention.

There are five cases which are "probably non-syphilitic." These include negative Noguchi reactions on four cases as follows:

1. A case of chronic alcoholism and alcoholic psychosis; 2. Alcoholic wet brain; 3. Alcoholic pneumonia; 4. Multiple sclerosis with negative history and clinical signs.

The one positive reaction was in a case of pyelonephrosis with uremia. As this patient was admitted to the hospital in coma, it would be unfair to lay any emphasis upon it.

An interesting feature so far has been the absence of a reaction in the five cases of chronic alcoholism cited.

General Summary and Conclusions.

Our results may be briefly summarized as follows:

1. A positive reaction was constantly obtained in inflammatory conditions of the meninges.

2. Spinal fluids obtained post-mortem invariably gave a positive reaction.

In reference to the value of the test in diagnosing syphilitic conditions:

1. In two cases of syphilis, one congenital, the other tertiary, the spinal fluid failed to give a positive reaction. Both cases were under active treatment at the time.

2. In ten cases giving no history or clinical evidence of syphilis, a positive reaction was obtained twice.

The Wassermann and Noguchi tests were done simultaneously on five cases. They were in agreement three times out of the five.

The details follow:

CLASS I.

(*a*). Actively Syphilitic.

Case XXII—27 years of age. Tertiary Syphilis. Noguchi negative.

(Abstract of case.) Patient had chancre eight years ago with secondary manifestations following, and was under treatment at that time for two months. Later he developed tertiary manifestations, including a syphilitic orchitis and gummata in the temporal regions. He was recently an inmate of Pav. A., Ward 1, Bellevue Hospital, suffering from gummata of the head, where he markedly improved under large doses of potassium iodide, with occasional doses of mercurial salicylate and calomel.

Case XXIII—Infant, 2 months old. Congenital Syphilis. Noguchi negative. (Wassermann.)

(Abstract of case.) One of a family of five children, of whom one is blind and another paralyzed. The most marked signs of syphilis included: 1, snuffles; 2, mucous patches in mouth and on buttocks; 3, desquamation on forehead, palms of hands and soles of feet; 4, a copper macular eruption about the anus and on flexor surfaces of legs; 5, excoriated and fissured lips; 6, greatly enlarged liver and spleen; 7, general glandular enlargement.

This child is still in the hospital and is receiving calomel gr. 1/10 t. i. d., with salicylate of mercury, gr. 1/3, every third day.

b) Non-Syphilitic.

		Noguchi		History	Clin. Signs
Case XXXI, Adult	Lobar Pneumonia	—	(Wassermann —)	—	—
Case XVIII, Adult	Lobar Pneumonia	—		—	—
Case XV, Adult	Alc. Cerebral Edema; Bronchopneumonia; Chr. Alcoholism	—		—	—
Case XXX, Adult	Sacral Abscess	—	(Wassermann —)	—	—
Case XXXIV, 2½ yrs	Tbc. Meningitis	+		—	—
Case XIX, 15 mos.	" "	+		—	—
Case XX, infant	" "	+		—	—
Case XXIII, 16 mos.	" "	+		—	—
Case XXIX, Adult	" "	+		—	—
Case XXXII, Adult	" "	+	(Wassermann —)	—	—
Case XIII, 6 mos.	Pneumococcus Meningitis	+		—	—

c) Probably Non-Syphilitic.

		Noguchi	Syphilis: History	Syphilis: Clin. Signs
Case IV. Adult	Chronic Alcoholism and Alcoholic Psychosis	—	X	—
Case XI, Adult	Alcoholic Wet Brain	—	X	—
Case VIII, Adult	Alcoholic Pneumonia (Lobar)	—	Cured Syphilis	
Case XIV	Pyelonephrosis and Uremia	+	X	—
Case XXI	Multiple Sclerosis	—	(Denied)	—

Class II consists of only two cases, both of which were non-syphilitic. The first, a case of pulmonary tuberculosis, gave a negative Noguchi and a negative Wassermann. The second, a case of adenocarcinoma of the stomach, admitted in coma, was at first suspected of being a paretic. Subsequent histological observations showed no lesions in the meninges or blood vessels that might be interpreted as syphilitic. This patient's spinal fluid was tested both ante-mortem and post-mortem, and a flocculent precipitate was obtained in about ten minutes in each instance.

SUMMARY OF CLASS II.

			Noguchi		Syphilis: Clin.	Syphilis: Anat.
Case XXVIII, Child	Pulmonary Tuberculosis	Antemortem	—	(Wassermann —)	—	—
Case II, Age 69	Adenocarcinoma of Stomach	Antemortem	+			
	Senility	Post-mortem	+		(Admitted in Coma)	—

Note: X History unobtainable.

There were eleven cases in which the fluid was tested post-mortem only. Of these, four were syphilitics, six were apparent non-syphilitics, and one should properly be classed as doubtful.

The four syphilitic cases (in all of which the diagnosis was based on the anatomical data) included: 1. Juvenile paresis with status lymphaticus; 2. Syphilitic meningitis with lobar pneumonia; 3. Syphilitic proctitis with erysipelas; 4. Syphilitic cicatricial stenosis of the larynx with edema of the glottis.

The six apparently non-syphilitic cases included: three cases of chronic cardio-valvular disease, one cardio-nephritic, one carcinoma of the esophagus with lobar pneumonia, and a case of chronic pulmonary tuberculosis.

The case classed as doubtful was one of cirrhosis of the liver with acute parenchymatous nephritis.

In every case of the entire series of eleven, non-syphilitic and doubtful, as well as syphilitic, there was a well-marked Noguchi reaction.

The appended summary gives the findings in a concise form.

CLASS III. (Fluid tested at Autopsy)

		Noguchi.	Syphilis.	
	Syphilitics.		History	Anat.
Case V, Age 12	Juvenile paresis, (4 hrs. P.M.) Status Lymphaticus	+	unobtainable	+
Case X (50)	Chr. Basilar Meningitis (Syph.) Lobar Pneumonia, (15 hrs. P.M)	+	unobtainable	+
Case XII	Facial Erysipelas Syphilitic Proctitis	+	(denied)	+
Case XVI	Edema of Glottis Cicatricial stenosis of larynx	+	unobtainable	+
	Apparent Non-Syphilitics.			
Case VI (39)	Chr. Cardio-valvular Disease Chr. Alcoholism, (6 hrs. P.M.)	+	—	—
Case XXIV (48)	Chr. Cardio-valvular Disease, (18 hrs. P.M.)	+	—	—
Case XVII (53)	Aortic Stenosis, (3 hrs. P.M.)	+	—	—
Case XXVI (50)	Cardio-Nephritic, (10 hrs. P.M.)	+	unobtainable	—
Case XXVIII	Carcinoma of Esophagus Lobar Pneumonia, (24 hrs. P.M.)	+ +	— —	— —
Case IX (29)	Chr. Pulm. Tuberculosis			
	Doubtful.			
Case III (53)	Cirrhosis of Liver Acute Parenchymatous Nephritis	+	(denied)	(scars on tibiæ)

PRESENTATION OF A CASE OF CYSTICERCUS CELLULOSÆ OF THE FOURTH VENTRICLE.*

Charles Norris, M.D.

The case was that of an Italian, 35 years of age. Since his immigration to this country, five years ago, he had always lived in New York City. Two months before his admission to Bellevue Hospital, in the service of Dr. James Alexander Miller, to whom I am indebted for the clinical history, he began to vomit after meals, the vomiting becoming more constant; and headaches set in, which became more and more severe. On admission the patient was fairly well nourished; there was constant vomiting and severe headache. Ophthalmic examination of the left eye showed a choked disc. The other eye examination was unsatisfactory. He was reported by the orderly to have died suddenly, several days after admission.

At autopsy, the convolutions of the brain were found markedly flattened, and with considerable distention of the cisternae at the base. The lateral and third ventricles were distended with clear fluid. On opening the roof of the fourth ventricle, a group of vesicles, composed of three cysts, the largest 5 x 7 mm., was found attached by a delicate pedicle to the wall of the fourth ventricle in its upper and lateral portion near the iter. There was considerable thickening of the ependyma of the iter and marked proliferation of the pia in the lateral processes of the fourth ventricle. A long worm, which was identified as Tænia solium, was found in the jejunum. No other noteworthy lesions except a chronic gastritis were found.

It is conceded that Tænia solium is the worm which infects man with cysticercus. The portal of entry is the intestine, as in this case. The ripe eggs entering the stomach during the regurgitation following vomiting (or a segment of the worm itself) are dissolved by the gastric juice, and the worm is set free from its shell and then penetrates the wall of the stomach. This mode of "auto-infection" of the worm was thought by Bruns to be the usual way in which a human being was infected. In only four of the seventy-two cases of cysticercus in the fourth ventricle, reported by Stern,† was a worm found in the intestine. Virchow, and practically all other authorities, believed that the infection occurs through the ingestion of uncooked meat or unwashed salads, etc. Owing to the habit of eating uncooked meat, the so-called "Finnen-krankheit" was very prevalent in Germany, before the meat inspection laws were in force.

Virchow reported that before 1885 one out of thirty-one bodies was infected by cysticercus. Henneberg's statistics (1903), compiled since the inspection laws were enforced, found the percentage of infected cadavers to be only 0.16 per cent. in Berlin.

The most interesting feature about the cysticercus disease of the fourth ventricle is the clinical history. The symptoms that are almost invariably present are headache, vertigo and vomiting. In 11 per cent. of the cases collected by Stern there were no symptoms. The disease has usually been diagnosed as tumor or hysteria, on account of the intermittent character of the symptoms. The cardinal point of diagnosis is that described by Bruns (1902), viz., the relationship of attacks of dizziness and of sudden death to sudden movements of the head.

The case was reported before sections of the cyst and its absolute identification had been made.

FILARIA IN SECTIONS OF INGUINAL LYMPH NODE.‡

B. C. Crowell, M.D.

The case for presentation refers to a native of the Danish West Indies, 32 years of age, who was admitted to the hospital service of Dr. Hayden for a swelling in the right groin, which he had had since a boy. He has been in this country six years. This swelling has been treated by cupping a few times with temporary improvement, and at one time, it was opened and a small amount of blood expressed.

* Reprinted from Proceedings of New York Pathological Society, New Series, Vol. X, Nos. 5 and 6, October and November, 1910.

† Ueber Cysticerken im vierten Ventrikel. Arthur Stern. Zeitschrift für klin. Medizin. Bd. 61, 1907, pp. 64-121.

‡ Reprinted from Proceedings of New York Pathological Society, New Series, Vol. X, Nos. 3 and 4, April and May, 1910.

He had large femoral and inguinal nodes on the right side, over which there was considerable edema. His right epididymis was enlarged, hardened, and nodular. There was some thickening of the right spermatic cord and evidence of moderate left-sided hydrocele. A few of the very large inguinal nodes were removed for diagnosis. On routine section of these, which showed a chronic hyperplastic lymphadenitis, there was discovered in a very much thickened and dilated lymphatic a section of what is apparently a nematode worm which corresponds to the descriptions of Filaria Bancrofti coiled on itself. It consists of a musculo-cutaneous margin enclosing a thin-walled bilobed uterus and an alimentary canal whose walls are pigmented. The uterus contains numerous ova and embryo filariæ, some of which can be seen outside of the parent worm in the lymphatic space. The lymphatics show very well the characteristic connective tissue and muscular thickening. Further examination of the patient was not made, aside from a single afternoon blood examination which showed no leucocytosis and 8.5 per cent. of eosinophiles.

Very few cases of such findings have been recorded. In 1900 Lothrop and Pratt reported finding of worms in the epididymis; and in 1901 Opie also found worms in the epididymis associated with an immense lymphatic varix involving the thoracic duct and all of the retroperitoneal lymphatics and extending into the scrotum. One other case of accidental finding of the parent worm in the hardened tissues was previously reported. Dr. James Ewing said that he had had a similar case at the Cornell Medical College six years ago.

EXTENSIVE THROMBOSIS OF THE CERVICAL VEINS FOLLOWING (a) ACUTE AND (b) CHRONIC OTITIS MEDIA.*

B. C. Crowell, M.D., and A. B. Eisenbrey, M.D.

(a) We are enabled to report the following case through the courtesy of Dr. H. M. Taylor.

B. L. I., male, 12 years of age, during convalescence from an attack of measles of average severity, developed a high irregular temperature with symptoms referable to a right-sided otitis media with mastoid infection. When the condition had continued for five days, operation was decided upon. It was found that the external jugular vein on the right side was thrombosed and that abscesses were present in the right hand and right ankle. In addition to the mastoidectomy and opening of the right lateral sinus, phlebectomy was performed and the abscesses were drained. After operation there was temporary remission of the acute symptoms, followed by recurrence and death on the fourth day.

Autopsy—Cause of death: Septicæmia (streptococcus); otitis media, acute suppurative, right side; thrombosis of lateral and petrosal sinuses, right side; thrombosis of cervical veins; pericarditis, fibrino-purulent; endocarditis, acute mural and valvular; acute parenchymatous degeneration and abscess of heart muscle; bronchopneumonia, terminal; acute splenic tumor; acute parenchymatous degeneration of liver; acute parenchymatous degeneration of kidneys; abscess of right hand, right ankle, and left gluteal region.

Smears from pus of middle ear showed numerous streptococci and a few staphylococci. Smears from lung showed a few streptococci, numerous pneumococci and large numbers of staphylococci. Culture of blood from heart showed a pure growth of streptococci.

The brain, with the exception of a small area of softening directly beneath the operative field, where the anterior margin of the right side of the cerebellum lay in contact with the lateral sinus, showed no macroscopic lesions further than a general congestion of the pial vessels. The cerebrospinal fluid was clear. No thrombosis of the cerebral vessels or abscess formation was found.

The longitudinal sinus contained considerable fluid blood and a small chicken fat clot. On the left side of the cranial cavity all of the sinuses were free and contained fluid blood. On the right side the lateral sinus contained a firm thrombus extending from the point where it had been opened into backward to the torcula, and anteriorly both petrosal sinuses were thrombosed. The middle ear on the right side

* Reprinted from Proceedings of New York Pathological Society, New Series, Vol. X, Nos. 3 and 4, April and May, 1910.

was the seat of an acute suppurative process which had extended backward into the cancellous bone. On the left side the middle ear appeared normal.

The heart contained fluid blood and in the right ventricle a small chicken fat clot was present. No thrombosis of the pulmonary vessels or infarction of the lungs was found. After removal of the heart, the superior vena cava was examined and found to contain a firm mass which, when grasped by forceps, was readily removed and revealed a thrombotic cast of the cervical veins. Unfortunately the early removal of the mass made it impossible to ascertain just which of the cervical veins were involved in the process, and dissection of the neck which might have revealed further evidences of thrombosis of the vessels was not undertaken.

The specimen presented consists of the cast of the cervical veins made up of the thrombus which was removed as previously described. Its appearance indicates that the process was more extensive and that, in removal, parts of it were broken off and remained in other branches of the vessels.

(b) The case for presentation is that of an Irish woman, 45 years of age, who about four years ago was said to have had an attack of meningitis, since which she had had marked loss of memory and had complained of her right ear, saying that it "felt as though stuffed up." At no time was deafness or a discharge noticed. She also had extensive ulcerations on the leg, which had been skin grafted. Her admission to the hospital was on account of her leg condition and while in the hospital she was regarded as a case of endocarditis, on account of the irregularity of the heart and the presence of a systolic murmur over the precordium.

At autopsy she was found to have an extensive thrombosis, involving the entire superior vena cava, both innominate, external and internal jugular veins, the right lateral sinus, and the temporo-sphenoidal and occipital veins. She had a chronic right-sided otitis media and mastoiditis; there was no cerebral or meningeal congestion or edema. The other lesions present were slight parenchymatous and chronic interstitial nephritis; double hydrothorax and nutmeg liver. The thrombi were old, definitely adherent, mixed thrombi, firmer and paler in the portions near the heart than in the cranial vessels.

Cultures made from the spleen and innominate veins show small curved and clubbed Gram positive rods, resembling pseudodiphtheria bacilli, but the relation of these organisms to the thrombosis was not determinable. Microscopical section of the innominate vein with thrombus shows an extensive chronic phlebitis, with loss of the endothelium at the point where the thrombus was attached, breaking up of the internal elastic layer and a considerable disintegration of the media with thickening and thrombosis in the adventitia.

A CASE OF PULMONARY STENOSIS.*

CHARLES NORRIS, M.D.

Dr. Charles Norris presented a case of pulmonary stenosis in a child 6 years of age, which up to within four weeks of death, had been in apparently perfect health. There was no history of syphilis or other previous illness except measles. A month before its admission to Bellevue Hospital the child's mother observed that its face was swollen, and from then on it ceased to play. It was taken to the hospital, where it rapidly developed general subcutaneous edema and ascites, but no pleural effusion. There was marked cyanosis.

At the autopsy there was found a tremendous hydropericardium, the pericardial sac occupying the whole anterior portion of the chest. The heart as a whole was about normal in size, but there was an extreme hypertrophy of the right heart. The right auricle was markedly hypertrophied with closed foramen ovale. There was a slight tricuspid stenosis with fresh, very minute verrucae. The pulmonary cusps showed an extreme stenosis barely admitting a small probe. The valves were large and greatly thickened and there was an extreme hypertrophy of the right ventricle, so much so that the normal relation as to size between the ventricles was reversed. The septum bulged into the left ventricle but was in no place defective. There was a slight nodular sclerosis of the mitral valve. The ductus arteriosus was closed.

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CALCIFICATION OF THE HEART MUSCLE FIBERS.*

ALWIN M. PAPPENHEIMER, M. D.

A most unusual site for the abnormal deposition of calcium salts is the striated muscle of the heart. Rokitansky in the third edition of his text-book (1856) describes an instance of this lesion in the following words: "the muscle-fibers were transformed into rigid, brittle, refractile rods." Von Recklinghausen refers to the condition, as does Orth in his Lehrbuch; neither writer gives a detailed description. The modern text-books either ignore the lesion, or content themselves with the mere mention of its possible occurrence. Hart (1), in a recent article, was able to collect but thirteen cases from the literature.

Besides the case here reported, we have seen sections from a case of Dr. Heinecke in Leipzig which showed an identical lesion; but in the routine examination of many hundreds of sections of heart muscle, we do not recall a similar finding.

The patient in our case was a male, 21 years of age. He was admitted to the service of Dr. Rogers at Bellevue Hospital in November, 1909, and operated upon for acute gangrenous appendicitis with peritonitis. Following the operation and continued drainage there was a general subsidence of all acute symptoms. On December 14, however, the patient developed a fecal fistula; on the following day his temperature rose, and from this time until his death, eight months later, he showed symptoms of chronic sepsis, with chills, high remittent fever, continued leucocytosis, progressive anemia and emaciation. Three operations for supposed subphrenic abscess failed to disclose the true condition. The medical treatment consisted in the administration of colon vaccines and thyroid globulins.

At the necropsy, there was found suppurative pylephlebitis, with recent thrombosis of the portal vein; multiple large abscesses of the liver; abscesses of the right lung; a large hypernephroma of the right adrenal, which showed a diffuse suppurative infiltration; a recent fibrinous pericarditis; marked degeneration of the kidneys, and a fecal fistula at the site of the old operation, walled off by adhesions.

The heart muscle is described in the protocol as being "extremely pale, soft, yellowish-brown."

The lime deposits in the myocardium of the left ventricle were discovered in the course of the routine histological examination. We can say nothing, therefore, as to the distribution of the calcareous areas, only a small piece being available for study. In all the sections examined, there were found sharply circumscribed groups of fibers impregnated with lime salts—as many as a dozen foci in a section roughly 1.5 by 0.5 cm. in size. The staining reactions are typical of lime salts; an intense blue with Delafield's hematoxylin, black with Heidenhain's iron hematoxylin, and with 5 per cent. silver nitrate after the method of von Kossa. Upon the addition of the acetic acid to an unstained section, there is no evolution of gas noted; carbonates, if present, cannot be demonstrated.

The calcification is sharply limited to the muscle fibers themselves, and even with the delicate silver nitrate method, no granules can be found in the interstitium. Either the deposit is in the form of coarse granules, which occasionally are arranged in transverse and longitudinal rows following the discs and primitive fibrils; or the entire fiber, together with its lateral anastomoses, is diffusely impregnated. The contours of the calcified fibers are somewhat irregular, and the calcareous fibers appear somewhat thicker than the normal fibers in the vicinity. On the cross section, one sees that the entire fiber is not always uniformly affected. The lime may be deposited first either in the centre or near the surface or in the form of scattered granules. In fibers cut longitudinally, only a segment of the fiber may be impregnated, or the process may be complete in one portion and but slightly indicated in another.

A careful study with Mallory's phosphotungstic and Heidenhain's iron hematoxylin stains has convinced us that the deposits of lime take place only in fibers which are the seat of advanced degenerative changes or complete necrosis. These necrobiotic changes are indicated by a loss of the transverse and longitudinal striations; by a pycnosis or complete disappearance of the nuclei; and by disintegration of the muscle substance into a structureless granular mass. Only the general contour of the fiber is preserved.

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These areas of focal necrosis—for such they are—are surrounded by normal muscle fibers with excellently preserved striations and normal nuclei. Aside from the lesions described, the myocardium is normal in all respects.

A point of importance is the absence of all inflammatory changes either in the areas of calcification themselves or elsewhere. In places there appears to be a slight proliferation of the nuclei of the perimysium about the calcareous fibers, and there may be found an occasional round cell. Of a true myocarditis, there is not a suggestion, and the lesion is distinctly not upon an inflammatory basis.

Calcification of the Heart Muscle Fibers.

Whether there is a relation between the deposition of lime and a previous infiltration of fat, could not be determined in this case because the material was preserved in alcohol. There is, however, no marked vacuolation of the fibers in the necrotic areas, nor did the appearance of the muscle in the gross suggest advanced fatty change. That there is no constant relationship between fatty degeneration of the heart muscle and calcification, is evident. The former is a most common, the latter amongst the rarest of findings. Hart has given consideration to this question. In his case, no fat could be demonstrated with Sudan in the calcareous fibers, although in the periphery of the necrotic areas, he found fibers showing considerable fatty change.

With potassium ferrocyanide and HCl, a few of the calcareous fibers take an intense blue color; the majority show only a diffuse bluish tinge. This finding is of interest in connection with the much debated question as to the relation between iron and calcification in the tissues. Hart (1) in his case, obtained a positive iron reaction in the calcified fibers, but ascribes no importance to his finding. Sumita (2) in his thorough work upon the relation of iron to calcification, also states that he obtained a positive reaction in calcified heart muscle. He gives no further details of his case, but his observation is important because he worked with iron-free reagents and took every precaution to avoid artefacts. The presence of iron in these cases is of interest since it is evidently not hematogenous in origin.

Of the histological changes in the other organs, we shall refer only to the deposits of lime found in the liver, adrenal tumor, lungs and kidney. In the liver, the lime was found in the form of granular masses in the walls of the abscesses. In the hypernephroma of the right adrenal, the tumor tissue was largely necrotic and infiltrated with pus. Here, as in the liver abscesses, lime was present in the suppurative foci. In the lungs, the lime was present in the form of globular or cylindrical masses of considerable size. These were situated either in the veins themselves—(old thrombi?)—or in the perivascular lymphatics. There was no calcification of the capillary walls or of the elastic fibers. In the kidney, several irregularly globular deposits of lime were found lying in the cysts beneath the capsule. There were also a few foci deeper in the cortex; in one place, the lime forms a cast lying within a Henle tubule. Most of the deposits are distinctly in the interstitial tissue.

In reviewing the reported cases of calcification of the heart muscle, we find that all authors agree that the deposition of lime is limited to the muscle fibers themselves, and to those only which show advanced degeneration. Fatty changes have been noted in the adjacent fibers, Roth (3), Hedinger (4), Wiechert (5), Hart (1), but not in those showing calcareous deposits. The collections of mono- and polynuclear cells which have been described about the calcareous areas, have been interpreted by a few writers as a primary myocarditis; more probably they represent a purely reactive inflammation about a calcareous foreign body, the lesion which precedes the deposition of the lime salts is a toxic necrosis of the muscle fibers.

The cause of the necrosis varies in the different cases. Hart's case was one of severe tertiary syphilis; Wiechert's, a case of paratyphoid A infection; Roth's, a case of phlegmonous inflammation; in Askanazy's (6) case, there was an ulcerative endocarditis. Langerhans' (7) observation of a case of calcification of the heart muscle in association with chronic plumbism, shows that inorganic poisons may play a role. In our own case, the long continued suppurative pylephlebitis is the obvious cause for the toxic degeneration of the fibers.

We do not wish to discuss at length the broader problems concerned in the abnormal deposition of lime salts in the tissues. It is well known, since Virchow advanced his theory of calcium metastasis, that many cases of generalized deposits of lime in the different organs have been associated with destructive bone lesions—malignant growths, suppurative processes, and so forth. A typical case of this category is that recently reported by Tschistowitz and Kolessnikoff (8), of multiple myeloma with extensive calcific deposits in the capillaries and elastic tissues of the lungs, in the glomeruli and membranae propriae of the kidneys, in the gastric mucosa, and in the media of various arteries. A similar case showing remarkable calcification of the endocardium of the left auricle, of the lungs and of the pulmonary veins, in a patient with myelogenous leukemia, has recently been reported by Versé (9) before the German Pathological Society. In cases of this sort the extensive halisteresis of the bones must be regarded as at least a contributory factor in the process. On the other hand, similar cases have been reported in which no destructive lesions of the bones could be demonstrated, and to which the idea of a "calcium metastasis" in Virchow's sense, does not apply. The experiments of Von Kossa (10) and of Rüdel (11) have shown that repeated injections of soluble calcium salts do not lead to calcification of the tissues.

On the other hand, there are many familiar examples of calcification associated with local necrosis of tissue, in which there is nothing pointing to an increased calcium content of the circulating blood, or to a failure in elimination. The calcareous incrustation of necrotic ganglion cells in the brain of general paresis is an illustration of calcification due to a purely local condition.

In the case here presented, there was no destructive bone lesion evident, although a complete examination of the bones could not be made. Furthermore, there is no reason to suppose on histological grounds that there was a failure on the part of the kidney or intestine to eliminate calcium properly, although only a chemical study of the excretions during life could have given us positive evidence of such an insufficiency.

All that we can say as regards the calcification of the heart muscle in this case is that it appears to be conditioned by a local necrosis of the muscle fibers; and for this local necrosis, we have sufficient cause in the long-standing pylephlebitis. The necrosis is apparently of toxic origin, and not due to infarction or to local myocarditis. The underlying cause for the calcific deposits in the lungs and kidneys is less clear, but in all probability they too are associated with similar local lesions of toxic origin. The lime deposit in the exudate of the chronic liver abscesses needs no special comment.

Addendum.

Since the publication of this paper, several articles and reviews have appeared, dealing with this subject. Bernhard Fischer (Frankf. Zeitsch. f. Path., Bd. 7, Heft 1. S. 82, 1911), described extensive calcification of the papillary musculature in an infant five weeks old, dying of aortic stenosis upon the basis of a fetal endocarditis. The calcification as in the other reported cases, was attended by extensive necrosis of the muscle fibers. Although round-celled infiltration and cicatricial areas of fibrosis were found beneath the endocardium and in other portions of the heart muscle, thereby establishing the diagnosis of fetal endocarditis, there was no evidence of inflammation about the necrotic or calcareous fibers. Fischer, therefore, believes with Hart and the writer that a toxic necrosis underlies the deposition of the lime salts.

Schilder (Ziegler's Beiträge, Bd. 46, Heft 3, S. 614) in a case of generalized amyloidosis, involving also the myocardium, found foci of calcification of the muscle fibers. There were no bone lesions. Although necrosis of the fibers was not recognized, Schilder thinks that the occlusion of small vessels through amyloid degeneration of their walls, may have brought about focal necrosis of the muscle cells, with secondary calcification.

In the interesting case of Beneke and Bonning (Ziegler's Beitrage, Bd. 44, S. 362) of local amyloidosis of the heart, no calcification of the fibers was present.

Siebenmann (Uber Verkalkung der Herzmuskulatur, I. D. Bern, 1909) has recently reported a case associated with osteomalacia. The original paper has not been accessible to me.

Experimentally, calcification of the heart muscle has been noted in rabbits, after repeated injections of influenza bacilli (Albrecht, quoted by Thorel), after injections of a diplo-streptococcus obtained from two cases of rheumatic endocarditis (Bracht and Wächter; Beitrag zur Atiologie und Pathologie d. Endocarditis Rheumatica. Arch. f. Klin. Med. 96, 5/6, 1907), and after prolonged feeding with horse, calf or beef liver (Lubarsch, Muench. Med. Woch. 1910, 30).

Thorel also repeatedly observed small isolated foci of calcification in the myocardium of inoculated cancer mice.

An excellent review of the entire subject, which does not, however, contribute new facts or viewpoints, is given in Thorel's Pathologie d. Kreislaufsorgane, Lubarsch and Ostertag's Erg. d.. allg. Path., 1910, 11th Albeitung, pp. 303-306.

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DOUBLE HYPERNEPHROMA.*

B. C. Crowell, M. D.

Dr. B. C. Crowell showed a large tumor which had been removed at autopsy from a patient at Bellevue Hospital. The patient was a young girl, 18 years of age, who had been admitted to the hospital in a practically moribund condition, so that but little history could be obtained. She said, however, that she had never been strong, though she had had no illness except typhoid fever. She had always been small. On admission she was found to be very much emaciated, the loss of weight having taken place within the last four months. During that time she had noticed an enlargement of the abdomen. She thought that at times her urine had been cloudy and bloody, and she had had some pain on urination.

At autopsy she was found to be much emaciated, with this very palpable tumor which lay on the left side practically displacing everything, the kidney being pushed downward. The growth did not originate in the kidney itself, which was apparently intact except for slight metastases in the lower pole. The tumor had undergone extensive necrosis, and aside from the general appearance there was a considerable amount of fluid which looked very purulent, as though infection had taken place. Section of the anterior part showed a tumor juice exuding from it on pressure. A similar smaller tumor occupied the site of the right adrenal, displacing the kidney tissue downward. The ureters and bladder were perfectly free; there was no ascending infection. The kidneys showed minute abscesses, and abscesses were also found in the intestine and spleen. Metastases were present in the kidneys, in the retro-

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peritoneal lymph nodes, and in the pleural viscera up to 3 cm. in diameter. Some very small nodules were found in the substance of the left lung. Section of the vessels was very unsatisfactory on account of the size of the tumor, so that whether or not there was tumor tissue in the renal veins or vena cava could not be determined.

The tumor was presented as a hypernephroma which was interesting on account of its large size, the two masses together with the kidneys weighing thirteen pounds.

A PRACTICAL IMPROVEMENT IN THE PREPARATION OF ANILIN-GENTIAN-VIOLET STAIN.*

JULIUS SHARNOSKY.

(*Laboratory Helper, Bellevue Hospital.*)

Paltauf's modification of the anilin-gentian-violet solution was called to my attention by Prof. William Elser. I have been unable to find any reference to a published description of the method, but learn that it has been in use for many years in Vienna.

The advantages of this staining fluid consist in the uniformity of its preparation, its permanence, and the absence of precipitate upon the slide. The formula for its preparation, and the time limits for the staining with this solution and with Gram's iodine solution and absolute alcohol (for all of which I am indebted to Dr. Elser) are as follows:

3-5 cc. Anilin, Merck's.
90 cc. Distilled water.
7 cc. Absolute alcohol.

Shake thoroughly; filter through moistened filter paper, and make sure that solution is clear. Then add

2 g. Gruebler's powdered Gentian Violet.

Allow fluid to stand for twenty-four hours, on account of precipitation which takes place. Filter before using.

The solution is good only when a metallic lustre develops on the surface of the fluid. This solution is said to keep from four to six weeks in a stoppered bottle which has been thoroughly cleaned.

Application:

Anilin-water gentian violet	3 minutes.
Gram's iodine sol	2 minutes.
Absolute alcohol, with stirring	30 seconds.
Weak carbol-fuchsin, or aqueous fuchsin	30 seconds.

The times stated above should be strictly adhered to, and the preparation should not be washed in water until the counter staining is finished.

The great importance of the anilin-gentian-violet stains in routine bacteriological work has led to a series of experiments with a view to improving them, especially with regard to permanency. The difficulty in preparing Gram's stain is well known. The disadvantage consists in not always obtaining a clear solution of anilin oil in water, the stain, when finally prepared, keeping at most two weeks, at the end of which period it begins to lake, complete deterioration taking place. In large laboratories the annoyance of continually having to prepare fresh stains, and the frequent necessity of waiting till a fresh product can be prepared, made the desirability of conducting experiments with the first stated view in mind most keenly felt.

As a result, a stain has been produced embodying both stability and ease in preparation. This was accomplished through the use of a salt of anilin, instead of

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* Read in abstract by Dr. Charles Norris.

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the base. This salt is a white crystalline body, much more soluble in water and in alcohol, yielding a clear solution, and possessing, at the same time, a higher grade of stability. The formula, as finally developed, is given below, together with a comparative table of the different anilin-gentian-violet stains in use.

Formula—Dissolve 3.5 g. of anilin hydrochloride (Kahlbaum's) in 90 cc. of water; add 10 cc. of absolute alcohol; warm to about 60° C. and add 1 g. gentian violet slowly, with constant stirring; digest over a small flame for about 10 minutes and filter.

It will be seen that the characteristic metallic luster develops at once, thus doing away with the necessity of waiting twenty-four hours before the stain is ready for use. The product prepared as above has kept ten months to date, without the slightest signs of deterioration.

Perhaps it would be advisable to say a word regarding the addition of 10 cc. of alcohol. In the old formulas, alcohol, of course, serves to facilitate the solution of anilin. But one may very properly question the necessity of using alcohol in our formula, in view of the solubility of the anilin salt in water.

If we start out with the premise that the anilin hydrochloride, when purchased, is absolutely neutral, there is no reason for the addition of alcohol. However, the commercial salt invariably has an acid reaction due to hydrolysis, rendering the addition of a few drops of anilin necessary to effect a neutral reaction (1), and it is thus apparent that the use of alcohol is desirable.

	Anilin.	Alcohol.	Stain.
Ehrlich's Anilin Gentian Violet (2)	2.5%–3%	15%	0.5%–1%
Ehrlich's Anilin Methyl Violet (2)	2.7%	8%	1%
Stirling's Anilin Gentian Violet (3)	2.3%	10%	1%
Paltauf's Anilin Gentian Violet (4)	3%–5%	7%	1%

Bellevue Pathological Laboratory:

	Anilin Hydrochloride.		
(Anilin Gentian Violet or Anilin Methyl Violet)	3.5% (Equivalent to 2.5% Anilin.)	10%	1%

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1. The term "neutral reaction" in this case is used from the standpoint of congo-red and fuchsin, and not as regards litmus or methyl orange.
2. Either gentian violet or methyl violet may be used in either of these formulas, although methyl violet, on account of its greater purity, is to be preferred.
3. Formula calls for 5g., but 1 per cent. (1g.) actually dissolves.
4. Formula calls for 2g., but 1 per cent. (1g.) actually dissolves.

PERIOSTITIS ALBUMINOSA.*

JOHN A. HARTWELL, M.D.

This condition was first described in a paper by Poncet, (1) published in 1874, from a study of cases seen by Ollier. Poncet described the clinical and pathological picture of the disease, gave the name of periostitis albuminosa to it, and considered it as a specific disease having no relation to other periosteal or osteal disease. Schlange, (2) in 1887, expressed the view that the disease is similar in etiology to suppurating periostitis, and that the peculiar exudate represents a degenerative change from the pus exudate, possibly because the infecting organism is attenuated. Volkmann, Kocher, and Tavel agree essentially with this view. Vollert (3), in an extensive study of the exudate, comes to the same conclusion. Bourlot (4) made an analysis of forty-eight cases. Of these he classed two as traumatic, three as tuberculous and forty-three as staphylococcic in origin. His view was that the disease was essentially the same as osteomyelitis, only differing from it in the nature of the exudate, and that this difference was due to the fact that the infecting organism was

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of a low grade of virulence. He compared the two from etiological, clinical and bacterial standpoints and demonstrated their close relation. Caillebar, (5) on the other hand, insists that all the cases are tuberculous in origin, and that the exudate is similar to the exudate occurring in tuberculous irritation of serous membranes throughout the body, and often seen in cold abscesses from bone and the soft parts. These selections from the literature, which is not extensive, express the various views as to the nature of the process.

The pathological anatomy of periostitis albuminosa does not differ essentially from other forms of periostitis, except in the peculiar exudate which gives to it its name. The irritating organism may be present in the bone itself, or it may be confined to the periosteum. Some writers have believed that the outer layers of the periosteum only were affected, but the greater number believe the condition to be subperiosteal in origin. Sections of the periosteum show the same inflammatory changes as are present in suppurating periostitis. The exudate, however, differs from pus. It is often free from any cellular elements. It varies in consistency from a thin, syrupy fluid to a gelatinous mass. It is transparent and straw-colored, or slightly more yellow. It contains a high percentage of proteid, often 3 per cent. and often coagulates spontaneously, this apparently depending, however, on the presence of leucocytes containing the prothrombin. The fluid is often large in quantity, and frequently forms a cyst-like cavity for itself in the soft parts. The soft tissues surrounding the bone usually show a marked inflammatory reaction to the irritation. The condition is rare, and we can find only two cases reported in the English literature, one on the dorsum of the fourth finger reported by Edington (6), and one by Dupuis (7) occurring on the tibia following an injury. Neither gives bacteriological findings. The following three cases coming under our notice during the past two years are deemed worthy of report:

F. S., on admission to the hospital, gave a history of a swelling appearing in the lower third of the left thigh about one month previously. No cause for this was known. The swelling was slightly tender and painful when walking, and there was some disability of the left knee.

Physical Examination—Gave some indefinite evidence of pulmonary tuberculosis. The lower two-thirds of the left thigh were uniformly enlarged down to the knee-joint, being three inches larger in circumference than the right thigh at corresponding points. The swelling interfered with the muscles in such a way as to prevent full flexion of the knee. It was slightly tender to pressure, and just above the internal condyle of the femur the skin was slightly reddened and here was the maximum tenderness. To palpation, the swelling was hard, and gave the sensation of a fusiform growth attached to the femur. It was slightly more marked on the internal aspect than on the rest of the circumference.

Operation—Incision was made over the inner aspect of the thigh, about three inches above the internal condyle. This was carried down through the muscles and a large quantity of thick, gelatinous fluid evacuated. It seemed to come from the medullary canal of the femur, through two fistulous tracts. A portion of the sac was removed for examination. It proved to be muscle tissue showing marked histological changes, of an inflammatory nature. The fluid planted on culture media gave a growth of staphylococci. The wound failed to heal and two weeks later the thigh was opened on its external aspect, and in carrying the incision down to the femur a large bone-like mass grew like a plate from the posterior surface of the bone, and spread out into the muscle tissue. It was separated from the soft parts by blunt dissection, and from the shaft by chisel leaving an apparently normal shaft intact, with the periosteum separated from the posterior aspect. It was then seen that what had been taken for fistulous tracts into the femur were, in reality, holes through this plate of bone. Subsequently the man made a good recovery.

Pathological Report: (Dr. Charles Norris)—The specimens removed at the first operation were small and unsatisfactory for diagnosis. At the second operation a considerable amount of tissue was removed consisting of muscle tissue and small and large bone plates and spicules. A half a test-tube full of clear, yellowish fluid was sent to the laboratory; this fluid clotted spontaneously in the course of half an hour. The examination of the various pieces show in the main an acute inflammatory process, varying, however, in different places as to histological detail. The muscle has undergone extensive hyaline degeneration. Some of the muscle cells show evidences of regeneration as indicated by multiplication of the nuclei. Many pieces, on section, seem to be made up of an edematous and very highly vascular tissue, the seat of extensive hemorrhagic and inflammatory edema. The serous exudate is in many places rich in plasma cells, with a small number of polymorphonuclear cells. In other places, the inflammatory process is less acute in character, showing small

and well circumscribed areas of small round cells and more or less dense masses of irregularly fragmented nuclei.

The pieces containing bone present a beautiful example of an active formative osteitis; the marrow spaces are lined with rows of osteoblasts and are filled with proliferating marrow tissue, showing numerous fibroblasts. This tissue without definite bone formation is extensive and in places so cellular in character that it gave rise to a question as to whether or not we were dealing with a pure type of ossifying periostitis. The clinical and X-ray features of the case seemed to lend support to the possibility of a tumor. The final diagnosis of the condition is ossifying periostitis of the femur with inflammatory lesions in the adjacent muscle and tissue. The term periostitis albuminosa refers to the character of the fluid obtained at the operation. The formation of fluid of this character is an expression of irritation of the periosteum.

We have placed under the microscope a section obtained from a case of sarcoma of the lower end of the tibia, which was treated with radium tubes by Dr. Abbe. The collection of fluid was under the periosteum of the lower end of the tibia in this case and was similar in character to that described in the case above. The formation of this fluid in this case was possibly due to the presence of a suppurative cellulitis resulting from the insertion of the radium tubes, the fluid having collected under a part of the periosteum not yet apparently involved by the growth. An important point to remember in diagnosis, is that the mere presence of such fluid does not exclude the possibility of a new growth.

W. P., male, 48 years of age. Gave a history of having noted a swelling in the upper end of the left tibia, which appeared about two years before, but it had given him no particular annoyance till he fell and struck it about three months before his admission to the hospital. Examination showed a fluctuating mass about the size of a small orange occupying the upper anterior part of the interosseus space of the leg. It showed the external evidences of being inflamed.

Operation—An incision into the mass evacuated a thick, gelatinous, semi-transparent fluid. It seemed to be encapsulated in a cystic wall. The patient remained well for nearly a year, when the swelling recurred, and this time it grew rather rapidly to its original size. It was again incised, and a cavity containing about eight ounces of a transparent, gelatinous material, varying in consistency from egg albumin to jelly, and of straw color, was found. This substance seemed to lie in a cavity bounded by the tibia, interosseous membrane, the fibula and the tibialis anticus muscle. There was no true sac. On the outer aspect of the tibia, near its head, was a roughened area denuded of periosteum, and the periosteum surrounding this was much thickened. A distinct bridge of bone grew from the tibia outward to the fibula resembling the bone plate described in the first case. The roughened surface of the tibia was curetted; the lining of the cavity was cauterized with carbonic acid, and firmly packed with gauze. A complete healing apparently took place.

The pathological examination of some of the wall of the cavity which was removed showed only chronic inflammatory changes. The bacteriological examination is not recorded. The Wassermann reaction for syphilis was positive in this patient.

D. M., 32 years of age. Suffered from typhoid fever in the fall of 1908. During his convalescence a painful swelling appeared over the outer side of the lower end of the humerus which was diagnosed as a periostitis. It never entirely subsided, but gave him comparatively little trouble for six months. Then it grew more rapidly and became painful. At the same time a second focus appeared over the subcutaneous surface of the tibia.

Operation—These were both opened in June, 1909. The lesion on the arm was found to be an osteomyelitis and periostitis involving the lower end of the bone. About six ounces of the same kind of fluid as was found in the other cases was present though it was slightly more turbid. The periosteum was thickened and separated from the bone for some distance. On opening the medullary cavity the medulla was found to be slightly purulent. The swelling over the tibia was incised, and gave exit to a similar fluid, but there seemed no involvement of the bone itself.

Pathological examination of the bone and the medullary substance from the humerus showed the changes of a subacute osteomyelitis. The fluid contained pus detritus. No bacteria could be demonstrated in it, and no growth developed on culture media.

These three cases are typical of the disease. They all involved the long bones. They all showed the characteristic fluid. They were all chronic. They all involved the under surface of the periosteum. Two involved the periosteum only, while one involved the medulla also. One showed a staphylococcus, one was sterile and the third is not recorded. One occurred without previous disease, one was in a syphilitic

subject, and one developed following typhoid fever. They would seem to demonstrate, so far as they go, that periostitis albuminosa is not a specific disease, but is an expression of an irritation of the periosteum by an infecting organism of a low grade of virulence which produces the characteristic albuminous exudate rather than true pus. We have no knowledge of why this is so.

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THE DIAGNOSIS OF INCIPIENT PULMONARY TUBERCULOSIS*

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Of the problems which confront the physician to-day none is more important and interesting than the diagnosis of incipient pulmonary tuberculosis. The chances for recovery of a tuberculous patient are in most instances, if not in all, in direct ratio to the earliness of the discovery of his disease; this fact alone should be a sufficient argument in favor of the employment of every means toward the detection of the affection in its earliest form. The importance, again, of diagnosis in the first stages of infection cannot be overrated from the point of view of social economy; it is costing the municipality and the State thousands of dollars yearly to care for subjects in the advanced stages of the disease, who, had their affection been diagnosticated in its incipiency, might be supporting themselves.

A discussion of the economic aspect of the question is outside the scope of this paper, but a consideration of the number of tuberculosis patients in our hospitals and other institutions whose support is derived wholly or in part from the public funds or from private charity is appalling; likewise the number of families which, because their older members are unable to exercise their earning power on account of tuberculous disease, receive aid from the community is no small one.

For the early diagnosis of pulmonary tuberculosis no unusual training is required; it is wholly within the attainment of the general practitioner who will use his powers to their full. And it is fortunate that this is so for most of the patients to whom this diagnosis is pregnant with importance apply, first, at least, to the class of physician who has come to be termed the "family doctor." There are, now and then, naturally enough, cases which present unusual difficulties but these are few among many. In the diagnosis of incipient pulmonary tuberculosis, as in that of any other disease, best results will follow a certain routine procedure. Each step in this procedure is of importance and particularly do I wish to emphasize this fact, for the diagnosis of tuberculosis in its early incipiency often cannot be assured until the results of these steps are reviewed and summed up.

1. *The History of the Patient*—This should be taken in full and with care; no detail of importance should be neglected. Heredity, to my mind, plays a much less important rôle in the causation of the disease than the fact that the patient may have had intimate association with tuberculous individuals. Such association may have taken place at home or elsewhere, the work-room, for instance. Trades of themselves seem to have no special etiological significance, but in the nature of things the affection is much more likely to attack those who work in crowded, ill-ventilated, and unsanitary quarters than those who are employed under the opposite conditions or in the open air.

The previous history of the patient with regard to former illness may teem with helpful facts: for instance, histories of influenza, pleurisy, pneumonia, and even of digestive troubles are often strongly suggestive of tuberculous lung disease.

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Surgical conditions, such as hip and spinal disease, cervical adenitis and anal fistula point distinctly toward tuberculous infection.

In eliciting the history of the patient's present illness the polymorphous character of the symptoms cited should not in any way be allowed to allay the suspicion of tuberculosis if there is the least reason for such; in fact by far the safest stand for the physician to take is to judge the patient guilty of tuberculous infection until, by every means at the examiner's command, he has been proven innocent of the disease.

Miller (1) gives the following as the more usual initial symptoms: 1.—Catarrhal or influenzal manifestations in which the cough is the chief symptom. 2.—Symptoms suggestive of malaria in which general malaise, loss of appetite, slight evening rise of temperature, and mild digestive disturbances appear gradually, with or without cough. 3.—Hemoptysis. This should always be held to be of tuberculous origin unless other distinct cause can be shown. 4.—Gastric disturbances which obscure other symptoms of more definite character. 5.—Anemia, without apparent cause. This symptom should not be allowed to deceive the diagnostician in young girls in whom chlorosis is so frequent. 6.—Pleurisy with effusion. This should always be considered tuberculous until the contrary is proven. 7.—Pain in the chest. This is a not infrequent initial symptom. It is usually dull and aching in character and often is referred to the shoulder blade. Miller holds that the combination of any two of these symptoms or trains of symptoms should, as a rule, be sufficient evidence to establish a tentative diagnosis. Even where definite physical signs are lacking suspicion should be kept alive and the physician should be stimulated to further careful observation of the patient and to regular and frequently repeated physical examinations. In such cases the time will often come when physical signs of certain diagnostic import will be detected.

2. *Physical Examination of the Chest*—As a preliminary, and a most essential one, the patient should be stripped to the waist and seated in a light room of which the temperature is sufficiently high for comfort; he should be taught how to breathe and to cough so that the auscultatory signs may be elicited to the best advantage. The inspection of the chest in incipient cases often offers no evidence of value. The main points on which observation should be centered are (*a*) the shape of the chest; (*b*) its symmetry; (*c*) its movement. One should notice whether both sides of the thorax expand synchronously, whether apices and bases show a correspondingly well-marked expansion, and whether there is abnormality of the general conformation of the chest. The supra- and infraclavicular regions are often little retracted until the disease is well advanced. A low chest expansion is of little diagnostic value.

Palpation may reveal changes in vocal fremitus; localized increased fremitus may indicate beginning infiltration or consolidation.

Percussion—Slight deviations from normal pulmonary resonance may be demonstrated, particularly at the apices, but they are often of such ill-defined character as to be of little diagnostic worth when not strengthened by other evidence.

Auscultation is the means which is to be relied on as giving the most valuable diagnostic testimony. Miller (1) states that cases in which one can, with certainty, demonstrate a lesion in the absence of abnormal auscultatory signs are very few. He considers the use of the stethoscope preferable to that of the unaided ear, for with it sounds unappreciable to the latter become plain; râles are more easily heard, and the instrument is better fitted for application to the various regions of the chest. The ear, of course, may be employed alone and aided by the stethoscope. At times the former is more acute in the detection of changes in the breath sounds. The portions of the chest over which abnormal physical signs are more likely to be demonstrated in early infections are: the supraclavicular fossæ; the first intercostal spaces, particularly at their inner and outer extremities; the region between the scapulæ just below the fourth dorsal vertebra; along the vertebral border of the scapula when the arm is thrown around and in front of the neck with the hand on the opposite shoulder, this area being over the interlobular septum; an area internal to the angle of the scapula; and, in children, the fifth and sixth spaces just external to the nipple. Miller suggests, as an aid to accurate auscultation, the use of a short, sharp cough alternating with a quickly expelled, short, quick inspiration; this should be employed previously to any deep respiration for the measurement of expansion in order that râles of evanescent character may not fail of detection.

By this method of auscultation the following observations may be made: 1.—The character of the breath sounds; 2.—The presence of râles and their character; 3.—The cough sound. The cough should never be omitted for, in itself, it has a character peculiarly its own; this may show the same variations as the breath sounds, and in addition it is essential for the appreciation of fine râles, which may not be audible at any other time. Also by its use we may be able to detect minute interruptions in

continuity which are not true râles, but are analogous to the change in breath sounds described as granular or rude breathing. The presence of this alteration in the respiratory sound indicates an early stage of the condition which later is evidenced by the presence of true râles. Changes in voice sounds may be demonstrated by auscultation. Alteration of the whispered voice tending toward the broncho-vesicular quality is evidence of slight consolidation; this change is appreciated more accurately by this sign than by either the true voice or the breath sounds.

The toxemia due to tuberculous infection is evidenced by an extremely important (from a diagnostic standpoint) train of symptoms, the most common of which are slight evening rise of temperature, rapidity of pulse, loss of weight, undue feeling of fatigue, increased rate of respiration, and anemia. These symptoms are of most value to the diagnostician when they are observed for a week or more under different conditions, at different hours of the day and especially before and after exercise. An important early diagnostic sign is a varying pulse rate and temperature. The latter may not rise greatly above the normal but its daily range is likely to be abnormally large. These symptoms and signs of toxemia, when taken in connection with a history pointing toward tuberculous infection, are of extreme diagnostic value even when unassociated with lung changes sufficiently marked to be demonstrable by physical examination.

Sputum Examination—In incipient pulmonary infections sputum examination is very likely to yield little diagnostic assistance, still it is important that frequent specimens should be examined and, while a positive result assures the diagnosis, repeated negative ones are by no means conclusive. Bacilli are said to be absent from the sputum in quite 65 per cent. of all incipient cases. Recently Paterson (2) has advocated treating the sputum with antiformin, which is a liquid composed of equal parts of liquor sodæ chlorinatæ and 15 per cent. solution of caustic soda, in the following manner: 10 c.c. of sputum are mixed with 2.5 c.c. of antiformin. The mixture is allowed to stand for twenty-four hours, when it is shaken and centrifugalized. The supernatant fluid is then drawn off and replaced with normal sodium chloride solution; this mixture is shaken and centrifugalized and the process is repeated. The sediment is then smeared and stained in the usual manner. He believes this process is a considerable aid in finding bacilli in specimens where they are few in number.

Hausmann (3) noting that many of his gastric cases gave evidence of beginning lesions at the apices, has examined the contents of their fasting stomachs (provided no sputum was obtainable) and in six cases within two months was able to demonstrate the presence of tubercle bacilli. This suggestion would appear worthy of further study, especially in connection with the use of antiformin and should be particularly applicable in children from whom it is often quite impossible to get specimens of sputum.

The inoculation of guinea pigs with sputum in which bacilli are not demonstrable is of value as a diagnostic help but is rather beyond the resources of the practitioner.

The stools are said to contain the bacillus, even in beginning tuberculosis, and examinations of them may reveal its presence.

Blood Examination—The statement made by Rosenberger that the blood of incipient cases often contains demonstrable tubercle bacilli is uncorroborated; in fact it is now believed that his results were due to the fact that his wash water was contaminated with an acid-fast bacillus morphologically similar to the tubercle bacillus.

Cytologic Diagnosis—Widal believes that a preponderance of lymphocytes in the blood speaks for tuberculous infection while a majority of polynuclear leucocytes of neutrophile and eosinophile types excludes the disease, but this theory fails of general acceptance outside of France. The employment of Arneth's method of differentiation of the nuclei of the leucocytes is being found to be of some value in diagnosis, but no definite work along this line has as yet been published.

The Opsonic Index—King (4) states that certain observations and experiments conducted by him and Inman (5) seem to show that opsonic index determinations may have a practical use in the diagnosis of early tuberculosis. Their complicated technique and the special knowledge necessary for their performance would seem to militate greatly against their general use. For diagnosis the relation of the temperature to the opsonic index before and after periods of exercise is observed. In tuberculous patients the temperature rises after exercise while the opsonic index is lowered. Jacob (6) finds that the opsonic index rises in pulmonary tuberculosis after a period of deep breathing lasting for about a half hour. He considers that this exercise produces an autoinoculation which results in a corresponding rise in the opsonic index and regards this method of great value in early diagnosis since by it the presence of infection can be demonstrated long before bacilli can be found in the sputum.

Agglutination Tests—These, according to von Ruck (7), may be relied on, either in connection with tuberculin tests or alone, to confirm the diagnosis in most non-bacillary cases where the physical signs are suspicious. Of 300 cases tested he found the reaction negative in 20, and in the rest positive in dilutions of from 1 to 5 to 1 to 50. Arloing and Courmount (8) have stated that agglutination in dilutions below 1 to 5 should not be considered diagnostic, but von Ruck believes that in the absence of other definite diagnostic evidence no reliance should be placed on a dilution less than 1 to 10. When subjective symptoms and physical signs point toward infection he is accustomed to consider a reaction in higher dilution of positive value and that the tuberculin reactions may be dispensed with since their results have always confirmed the serum tests in his experience.

The Tuberculin Tests—Of these there are four, three of which have been introduced comparatively recently.

1. *The Percutaneous Test*—This consists in the inunction of an ointment of equal parts of old tuberculin and lanolin. The site of the inunction is usually a small area of the skin over the abdomen. A positive reaction is evidenced by the appearance of a papular eruption. Bandelier and Roepke (9) believe that this test is inferior in its certainty to the cutaneous test which is uninfluenced by the thickness and dryness of the skin, the number of its pores and various constitutional conditions, factors which materially affect the percutaneous test. The field of the latter is in infants in the first half year of life and in these a positive reaction points strongly toward the probability of an active tuberculous infection.

2. *The Conjunctival Test*—This consists in the instillation into the eye of a drop of a ½ to 1 per cent. solution of old tuberculin in normal NaCl. A positive reaction is evidenced by a varying degree of congestion of the caruncle and conjunctiva which appears in from three to forty-eight hours. This test is a reliable test for patent bacillary tuberculosis and as such it is superfluous. It does not show whether the process is active or inactive. A negative reaction does not prove the absence of active tuberculosis and positive reactions may appear in healed tuberculosis, in the clinically nontuberculous, and in the healthy. As a rule the test does not react positively in those immune to tuberculosis or in the cachexias of tuberculosis and other conditions (9). The disadvantages of the conjunctival test are that it cannot be employed if there is any inflammatory condition present in the eye and that it may cause untoward results. Both it and the percutaneous test are at present generally discarded.

3. *The Cutaneous Test*—This consists in the inoculation of a small scarified area of the skin preferably upon the arm, with a drop or two of a 10 to 25 per cent. solution of crude tuberculin in salt solution (or 5 per cent. carbolic-glycerin, 1 part; normal sodium chloride, 2 parts). A positive reaction is evidenced by the appearance in from twenty-four to forty-eight hours of a zone of light pinkish redness about one-half inch wide and accompanied by swelling; finally a papule forms which disappears in from seven to eight days leaving behind some temporary discoloration of the skin. The advantages of this test are (9) that it is simple, harmless, applicable to febrile and bed patients, and causes no local or constitutional disturbance. A positive result does not point out the site of the lesion, nor show whether the process is active or inactive. It may appear in the clinically nontuberculous and indicates that the body at some time and in some manner has been infected with the tubercle bacillis. Cases in which positive reactions occur and in which no lesion is demonstrable may be accounted for on the ground that the lesion, being insignificant, has been overlooked. A negative reaction points strongly toward freedom from tuberculous disease, but on the other hand the reaction may remain negative in the presence of actually existent and clinically demonstrable tuberculosis. Negative results may occur also in certain constitutional conditions, such as general cachexia, and in idiosyncrasy of the skin or the exanthemata. The positive result is of specifically tuberculous nature and its occurrence points toward pathologically existent tuberculosis.

The great field of usefulness of this test is in children and in them a positive reaction is an evidence strongly in favor of the existence of tuberculosis. In adults a definite and promptly appearing reaction is moderately good testimony in favor of recent and active infection. Mild, delayed, and atypical reactions are valueless in diagnosis since healed foci which have never given definite signs or symptoms may be evidenced by positive reaction. The negative value of the test is impaired to but slight degree by the exceptional cases of tuberculosis which fail to react for the reasons given above (1).

Baldwin (10) considers the cutaneous test to be the one most suitable for general use, and that it is absolutely harmless. No other test is required for children, because in them a positive reaction is more significant of recent infection and does not often occur in apparent health under the age of 12. Other tests may be necessary in adults

to confirm the result of a cutaneous test, but this latter can be advantageously employed as a preliminary in all cases.

4. *The Injection or Subcutaneous Test*—This is the last resource and the most searching method of tuberculin diagnosis (10), and for this reason it is often regarded as the only satisfactory test, in spite of the unpleasant fever reaction. Baldwin (10) regards it as unnecessary in most cases at present, but in instances where a focal reaction is desired, for instance, where a negative cutaneous test requires confirmation it is of great value. Since the focal reaction in the lung escapes notice in most suspects, the subcutaneous test is of doubtful value in confirming the positive cutaneous reaction.

The most satisfactory tuberculin to employ is Koch's original product, but other filtered extracts may be used. Preparations containing dead bacilli should be avoided; the same is true of emulsions or vaccines, owing to their uncertain and irregular absorption.

Klebs (11) advises the following technique: The site of the injection, which may be under the angle of the scapula or other suitable point, is sterilized, as is also the needle to be used, and the solution of Koch's old tuberculin, diluted with 0.5 to 0.25 per cent. carbolic acid in distilled water, is injected deeply into the tissues. The initial dose differs—Brown advises 0.5 mg., to be followed, if no reaction takes place, successively by 1, 3, 5, and 8 mg. Roepke employs 0.2, 2, and 5 mg. The dose in children must be smaller by 1/10 to ½ than in adults. The reaction appears in 6 to 8 hours as a rule, hence 8 to 10 A. M. is perhaps the best time for the injection.

A positive reaction (9) consists of four phases: 1.—The local inflammatory reaction at the point of injection; 2.—The rise of temperature; 3.—The constitutional disturbance, headache, malaise, prostration, nausea, etc.; 4.—The inflammatory reaction in the tuberculous focus. These may appear simultaneously, separately, or two or more in combination, and differ in their diagnostic value; by some the pyrexia and constitutional symptoms are considered most significant, while others hold that the focal reaction is more pregnant with meaning. If one dose produces a mild indefinite reaction the same amount may be given after two to three days, but the dose should not be increased; Koch regards a strong reaction following a repeated dose as especially characteristic and an almost infallible sign of tuberculosis. The interpretation of results must take into account the amount of tuberculin required to produce the reaction, the promptness with which it develops, and the extent of the local and constitutional sequelæ.

In applying this test care should be taken that the tuberculin solution should be freshly made and accurately measured.

The contraindications are as follows. 1.—A febrile temperature; the temperature should not have risen above 99.5° F. in the mouth for at least three days before the test. 2.—The test should not be employed when a satisfactory diagnosis can be made without it. 3.—Rapid pulse. 4.—History of recent hemoptysis. 5.—Organic heart disease. 6.—Kidney disease. 7.—Epilepsy. 8.—Addison's disease. The test is inadvisable in hysteria, convalescence from any severe illness, apoplectic habit marked arteriosclerosis, diabetes, and amyloid degeneration of the viscera.

The subcutaneous test is the diagnostic test of final resort and is the most certain of the tuberculin tests. Like that of the other tests its clinical value is usually in direct proportion to the smallness of the dose and the degree of the response. The more recent the infection and the more extensive the disease the more delicate is the reaction unless the disease is rapidly progressing or grave constitutional weakness is present (10). In general it may be stated that the tuberculin tests are very valuable when taken in connection with the patient's history, his physical signs, and his constitutional symptoms.

X-Ray Diagnosis—Klebs (11) considers the fluoroscope of little use as an aid in diagnosis in most instances: at times it will show a contracted shaded apex when dullness and marked changes in breathing cannot be discovered, but this is the exception rather than the rule. Limitation of motion at the base is more commonly to be detected and is more valuable as a diagnostic sign, but too much importance should not be placed upon it. The fluoroscope is of very material aid in the early diagnosis of bronchial gland enlargement, and consequently has a distinct field of usefulness in suspected cases in children.

Rist (12) believes that an increased shadow at an apex may be due to active or old disease or both. When there are symptoms and signs of infection at an apex without an increased shadow on the plate he suspects a fresh involvement in its early stage. A diminished shadow at an apex with no physical signs may indicate active commencing tuberculosis. Radioscopy excels physical examination in its ability to show the extent of pulmonary disease. Beginning central foci are not demonstrable by physical examination, but the X-ray may detect them.

Woiff (13) holds that the X-ray, in connection with the tuberculin test, enables us to locate the lesion when the latter has proven its existence, the ray being of special value where physical signs are equivocal and the symptoms are suspicious.

Krause (14) finds that in early tupberculosis in adults the fluoroscope will detect apical infiltrations which are recognizable on percussion. The X-ray examination is likely to show that the lesion is more extensive than percussion would lead one to suspct. Infiltrations either not demonstrable by percussion or only indefinitely so can often be detected by the fluoroscope, and, when doubtful, confirmed by X-ray photographs. Neither the fluoroscope nor the X-ray photograph will detect early catarrhal processes, but when these are of long standing the apices may show darkly owing to their poor aeration. These shadows do not clear up on inspiration. Diaphragm pictures may demonstrate the presence of incipient infiltrations which would not be shown by other methods. Calcification of the first rib can be detected, and, according to Freund, is an aid in early diagnosis. The clearing of the apices on inspiration which is present in health is often absent in early tuberculosis. The alterations in movement of the diaphragm are of no diagnostic value.

In incipient infections in children and young people apical findings are lacking, hence detection of shadow changes at the hilum of the lung, such as enlarged, indurated, infiltrated, calcified, or caseous bronchial glands or similar processes in their neighborhood, are the more important. Such findings are of extreme value in early diagnosis, but we must depend on the clinical findings to learn whether these processes are active or no.

The great drawback of the X-ray examination in pulmonary affections is the fact that considerable skill is necessary to the proper interpretation of the findings.

Summary—When it comes to the making of a diagnosis in a case of suspected incipient pulmonary tuberculosis the following factors seem to me to be the most important and the ones on which chiefest dependence is to be placed:

1. The anamnesis. A history of association with other cases of tuberculosis and of previous illnesses such as would point to pulmonary infection is very suggestive.
2. Proper, thorough, and, if necessary, frequently repeated physical examination.
3. Careful observation of the symptoms of toxemia.
4. The cutaneous tuberculin test.
5. X-ray examination.
6. As a final recourse, a diagnostic injection of tuberculin.

I have omitted sputum examination from this list because positive results are so infrequent in beginning infections, and because negative results are absolutely inconclusive.

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A CLINICAL STUDY OF THE CHILDREN OF TUBERCULOUS PARENTS.*

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This report is based upon the careful examination of 150 children whose parents were under treatment for pulmonary tuberculosis at the Bellevue Hospital Tuberculosis

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Clinic. The examinations were made as a part of the routine of the clinic work in an endeavor to supervise these families and to discover unsuspected cases of tuberculosis.

The children observed lived in tenements, in most instances under insanitary conditions and in close association with their parents, the majority of whom had pulmonary tuberculosis in an advanced stage. With few exceptions the children were sent for examination to the clinic, not because of any symptoms of which they complained, but simply as a routine procedure on the part of the visiting nurse.

Their ages varied from 2 to 15 years, with an average age 8½ years.

Basis of Diagnosis.

The difficulty of diagnosis in such cases is easily appreciated, but as preventive work of this sort marks the line along which progress in our knowledge of tuberculosis must proceed, our endeavors to reach a definite diagnosis in these cases may be of interest and of value.

The most important factors in diagnosis may be summarized as follows:

1. The tuberculin tests.
2. Pulmonary symptoms and physical signs.
3. Sputum examinations.
4. Joint, bone and other non-pulmonary lesions.
5. Malnutrition.
6. Hypertrophied cervical lymph nodes.
7. Hypertrophied tonsils and adenoids.

A diagnosis can be reached only by a consideration of all of these factors taken together, and on this basis we have classified our cases into

A.—Positively tuberculous.

B.—Doubtful cases.

C.—Not tuberculous.

A. Positively Tuberculous Cases—In this class are included, 1, all cases in which there are positive typical signs in the lungs or demonstrable joint or other non-pulmonary lesions elsewhere in the body; and, 2, all other cases in which there are suspicious symptoms, such as malnutrition, persistent cough or inconclusive physical signs in the lungs which react positively to tuberculin.

B. Doubtful Cases—These include cases of, 1, all children in whom tuberculin tests were not made, who showed constitutional or pulmonary symptoms or irregular signs in the lungs, or who showed distinct malnutrition without any other symptoms or physical signs; and, 2, those of all apparently healthy children who react to tuberculin.

C. Non-tuberculous Cases—We have placed in this class, 1, all cases in which tuberculin tests were made and in which there was no reaction; and, 2, all cases in which no tuberculin tests were made and in which the children showed no symptoms or physical signs and were of normal weight for their age.

It is immediately evident that in a large number of cases we have employed the tuberculin tests as the determining factor in diagnosis. Our reason and justification for so doing will be discussed later.

Results—Of the 150 cases examined, the results according to the above classification were as follows:

1. Positively tuberculous, 76 cases, or 51 per cent.
2. Doubtful, 31 cases, or 20 per cent.
3. Not tuberculous, 43 cases, or 29 per cent.

These results, showing that more than one-half of the children examined were positively tuberculous, are so astonishing that they can be accepted only after the most rigid scrutiny of the methods which we have employed. This we have attempted to accomplish by careful analysis of our findings, studying separately each of the various factors which have been used in establishing the diagnosis.

Factors in Diagnosis.

1. *The Tuberculin Tests*—One hundred and thirteen of our subjects were tested with the ophthalmic and the cutaneous tests. In 38 of these cases the results of the ophthalmic and cutaneous tests were controlled by the hypodermic tuberculin test.

The ophthalmic test was made with a 1 per cent. solution of crude tuberculin in sterile salt solution, following closely the method and system recommended by Baldwin.

For the cutaneous test we used varying strengths, 10 per cent., 25 per cent. and 50 per cent. of crude tuberculin in sterile salt solution. Only the results obtained

with the 10 per cent. and 25 per cent. solutions are, however, considered here. In no case in which the 50 per cent. was positive was the 25 per cent. negative.

In the hypodermic method we have considered 5 mg. as the maximum diagnostic dose, and in the great majority of our cases in which reactions were obtained it was not necessary to go above 1 or 2 mg.

Of the 113 children tested with tuberculin, 74, or 65 per cent., reacted positively.

In 95 cases the ophthalmic and the cutaneous tests were made in the same individual. The results of these two local tests were identical in all cases but 10. In 9 of these cases a cutaneous reaction occurred without any corresponding ophthalmic reaction. Four of the children were subsequently tested hypodermically and all reacted.

In the remaining case, which was that of an overgrown boy of 15 years of age, the eye reaction occurred without a skin reaction. This suggests a confirmation of the general impresssion that the cutaneous test is more reliable in children than in adults.

Recurrence of the local reaction both in the eye and in the skin during a reaction to the hypodermic test, given from three to five weeks later, was noticed in several cases.

We have been fortunate in encountering none of the permanent or serious injuries from the ophthalmic tests which have been reported by other observers, but some of our reactions were very severe and prolonged. Only one skin reaction was sufficiently severe to cause discomfort to the child. This one went on to slight suppuration and the formation of crusts resembling closely the vaccination pustule. In this case, however, we could not positively eliminate the possibility of a secondary infection from scratching.

Since we have employed the scarifier, suggested by von Pirquet, our cutaneous reactions have been on the average less severe.

Comparative Value—The ophthalmic test is more apt to meet with resistance from the child, and in the case of such resistance it can not be performed as carefully and thoroughly as the skin test, which, of course, militates against an accurate result. This is especially true in case the child cries. Under these circumstances a considerable portion of the fluid instilled will be washed out of the eye. This reaction, moreover, is frequently very transitory, disappearing within twenty-four hours, and in the event that the child does not return within that time for examination, the possibility that a positive reaction has escaped notice always remains.

To accept a parent's statement as to the results of the test is, of course, to render its value entirely negligible. Even to have a nurse visit the homes, either of all the patients tested within the first twenty-four hours, or simply the homes of those children who do not present themselves for examination at the clinic at the time ordered, is not satisfactory or reliable. The diagnosis of a reaction, which is at times so delicate as to be influenced even with a trained physician by the "personal element," should be made only by the physician himself.

The cutaneous test, on the other hand, is open to none of these objections. It can be detected in the great majority of cases for at least five to seven days after the inoculation, and in well-marked cases pigmentation and scars remain at the site of the inoculation for a considerably longer period. Moreover, in a certain number of children who are seen early after inoculation a skin reaction occurs without a corresponding eye reaction.

The following facts seem to justify us in considering a positive skin reaction as presumptive evidence of tuberculosis in children.

1. Of 9 children with positive typical physical signs of pulmonary tuberculosis in whom the test was made, all reacted.

2. Of 73 children with suspicious pulmonary symptoms, 80 per cent. reacted. Of 40 children without such symptoms only 40 per cent. reacted.

3. Of those with physical signs in the lungs, both typical and atypical, 82 per cent. reacted; of those with no physical signs, only 48 per cent.

4. Of those whose nutrition was below par and had in addition cough and physical signs in the chest, 88 per cent. reacted. Of those children of normal weight and without pulmonary symptoms or physical signs, only 25 per cent. reacted.

5. In the 38 cases controlled by tuberculin injections there was no discrepancy between the cutaneous and the hypodermic tests in any case. Nine of these subjects were negative and 29 positive to both tests.

It should, of course, be borne in mind that not every subject reacting to the local tuberculin tests is necessarily in need of active treatment as a case of tuberculosis, though such cases should be kept under careful observation. Given a tuberculin reaction in an apparently healthy child, the course to be pursued should depend on the course of the case under close supervision.

2. *Pulmonary Symptoms and Physical Signs*—Eighty-seven of our children, or 58 per cent. of all, gave a history either of protracted cough or of coughs and colds recurring with unusual frequency. Of these 87 a positive diagnosis of tuberculosis was made in 65 per cent.

Seventy-three children had normal physical signs in the lungs, and of these 72 per cent. were positively tuberculous according to our classification.

On analyzing the physical signs it is interesting to note that only 15 children had the apical signs usually accepted as being typical of pulmonary tuberculosis in adults, and that all of these 15 children were over 9 years of age. The other 58 children had physical signs which have not been generally accepted as typical of pulmonary tuberculosis in children, or, we might say, as of even suggesting it.

The most important of these signs are fine localized subcrepitant râles situated in some portion of the lungs other than the upper portion of the upper lobes. These râles were present in 35 cases and occurred usually without any change in the percussion note or breath sounds. In most instances, 28 cases out of the 35, they were found in the region of the nipples, usually in the fifth or sixth intercostal spaces just without the mid-clavicular line. In two-thirds of the cases they were on the left side. In a few cases they occurred on both sides.

These râles differ very decidedly from the râles of atelectasis in that they do not disappear on coughing or deep inspiration. In most instances they are constant, being heard consistently on several repeated examinations. In a few instances they were inconstant or were developed during the course of a tuberculin reaction. In almost no cases, however, were they audible over a period of several months' duration.

The area over which these râles were distributed varied from that which could be covered by the bell of the stethoscope up to that larger than a silver dollar. In a few cases a gradual decrease in the size of the area or a diminution in the number of the râles heard over any one area could be traced in conjunction with the improvement of the particular case under treatment.

The presence of these râles we consider very suggestive of a tuberculous focus in this situation, the infecting bacilli probably being carried to this point by the lymphatics from the bronchial glands about the root of the lung.

We have not attempted to decide what might be the extent or exact character of the pulmonary lesion which these physical signs represent. Autopsy reports on infants and young children dying from pulmonary tuberculosis show that marked discrepancy between the physical signs and pulmonary lesions very frequently exists, so that it would be hazardous to predicate from the physical signs what the exact pathologic findings might be.

Careful X-ray examinations might be of service in such cases, and we are planning to have such examinations made in the future.

In addition to the 35 children who showed these fine râles above described, there were in our series 23 who exhibited sibilant and sonorous râles over the lungs. These râles were localized in various portions of the chest in 10 cases. In the other 13 cases they were more or less generally distributed.

Of these 58 cases with atypical signs, that is, with the localized subcrepitant râles and the sibilant and sonorous râles, signs which are not generally accepted as typical of pulmonary tuberculosis, a positive diagnosis of tuberculosis was made in 39 or 67 per cent. Nine subjects were considered doubtful, and 19, or 17 per cent., were not tuberculous. Further analysis shows that of the 35 cases in which there were localized fine râles a diagnosis of positive tuberculosis was made in 74 per cent., of those with fine râles near the nipples in 82 per cent. Ninety-two per cent. of these children on whom tests were made reacted positively to tuberculin. Of the 23 children who had sibilant and sonorous râles, 56 per cent. were considered positively tuberculous. In 10 of these cases these râles were localized and here 80 per cent. were tuberculous, as against 35 per cent. of the remainder in which the râles were generally distributed over the chest.

Considering the constitutional condition and the pulmonary signs together, we find 39 cases in which abnormal physical signs and general malnutrition were associated. In these 31 children, or 79 per cent., were tuberculous, 2 were doubtful and 6 not tuberculous.

We believe that the physical signs in the chest above described as being atypical signs of pulmonary tuberculosis are found sufficiently frequently in children to warrant their acceptance as very significant in weighing the question of a diagnosis of tuberculosis. Taken in connection with the tuberculin tests, they produce a definite clinical picture in many cases. If this is true, it undoubtedly follows that pulmonary tuberculosis in children is far from being an uncommon form of the disease. The course of the disease in these cases is not at all that which is usually described as

being the common one in tuberculosis in children. The symptoms as well as the signs are few, the progress of the disease very slow, and both signs and symptoms clear up in a majority of cases under appropriate treatment, that is, taking the children out of school and keeping them in the open air.

The frequency with which we have encountered these cases suggests strongly the possibility that it is these cases in which the tuberculosis lesion, remaining latent during childhood for many years, may break out into adult phthisis later in life. This hypothesis would fit in very well with modern notions of the frequency of tuberculous infection during childhood. Certainly in this series of cases those children who reacted to tuberculin showed more often these pulmonary signs and symptoms than any other evidence of disease elsewhere in the body.

3. *Sputum Examinations*—Very few of the children expectorated and sputum examinations were made in only 16 cases. In only one of these were the tubercle bacilli found. In a few cases the method advocated by Holt, of exciting a cough and catching the sputum brought into view on a swab, was attempted. In no instance did it give a positive result.

These findings do not accord with those recently published by Holt and others. Their patients, however, were in hospital wards and were acutely sick, many of them finally dying of the disease. Ours, on the other hand, were only slightly ill, their parents usually not being aware that there was anything wrong with their children except perhaps that they were delicate or poorly nourished.

It is possible that by the inoculation of guinea-pigs by fresh specimens of sputum from these cases a larger number of positive results might be obtained. It is our hope to carry out some investigations along these lines during the ensuing year.

4. *Joint, Bone and Other Non-pulmonary Lesions*—Ten children in whom the diagnosis of tuberculosis was made showed evidence of tuberculous lesions elsewhere than in the lungs.

In 2 cases there were scars in the neck anterior to the sterno-mastoid muscle. These resulted from the closure of sinuses of previously suppurating glands, presumably tuberculous, inasmuch as the suppuration did not occur at the time of any acute infectious disease. In one of these cases pulmonary signs were present. Both children reacted to tuberculin, to the hypodermic as well as to the local tests.

Five other children each had one or two markedly enlarged cervical glands which were considered tuberculous, and one of these had pulmonary signs as well. Tuberculin tests were made on the other 4 children without pulmonary signs. All 4 reacted.

Of the 3 remaining children, 1 had tuberculosis of the hip, 1 had a tuberculous dactylitis and a scar resulting from a tuberculous ostitis of the radius, and the last had tuberculous peritonitis and enteritis. The last had pulmonary tuberculosis as well. Alll three reacted to tuberculin.

In view of the opinion generally held concerning the relative frequency of pulmonary and other forms of tuberculosis in children, it is worthy of note that out of 76 cases of the disease chosen at random, but 10 of them should show non-pulmonary lesions, and even more so that but 7 of these, or but 8 per cent. of the total number of cases, should show tuberculous lesions without any pulmonary involvement.

5. *Malnutrition*—One hundred and seven children of our 150 were under the standard weight for their age. Of these, 62, or 58 per cent., were tuberculous; 19, or 18 per cent., were considered doubtful, and 26, or 24 per cent., were non-tuberculous.

Eighty-two of the 107 were tested with tuberculin; 56, or 68 per cent., reacted. Of 31 children whose weight was normal only 18, or 59 per cent., reacted.

Of children with symptoms and malutrition, 48 per cent. of those tested reacted. Of children with symptoms but with no malnutrition, 36 per cent. reacted.

There were 50 children with physical signs in the lungs and malnutrition. Of 42 of these tested, 36, or 85 per cent., reacted. Of 21 with signs in the chest and without malnutrition, 16, or 76 per cent. reacted.

In 41 cases were symptoms and signs and malnutrition associated. Of 34 children tested, 30, or 88 per cent., reacted. Of 13 children with symptoms and signs without malnutrition, 9, or 69 per cent., reacted.

Of 24 children tested with no symptoms or signs but poorly nourished, 9, or 38 per cent., reacted. Of 8 children tested with no symptoms or signs and of normal weight, only 25 per cent. reacted.

Of these 9 children with no pulmonary symptoms or physical signs in whom a diagnosis of tuberculosis was made, there were non-pulmonary tuberculous lesions present in 5. In the other 4 cases the diagnosis was made on the malnutrition together with a positive tuberculin reaction.

From the figures given above it would appear that the presence of faulty nutrition in a child in whom tuberculosis is suspected renders the existence of this disease more probable, inasmuch as in the children suffering from malnutrition in addition to presenting symptoms and physical signs, a much greater proportion were found to be tuberculous than of the same class of children whose weight was normal.

In children who can be kept under observation over a considerable period of time an approximately stationary weight during this period is even more suggestive of tuberculosis than the mere presence of faulty nutrition, provided that in them we have any reason to be suspicious of the existence of the disease. Actual loss of weight over such a period is extremely suggestive.

In 100 cases in which the height was measured, 73 children were under the standard weight for their height. Of these 31, or 42 per cent., were tuberculous; 23, or 32 per cent., were doubtful; 19, or 26 per cent., were not tuberculous.

6. *Hypertrophied Cervical Lymph Nodes*—We have classified as hypertrophied those cervical lymph nodes which were palpable and at least the size of a small pea. Palpable nodes apparently smaller than this are not included as being hypertrophied.

In our cases we found 79 children in whom the cervical glands were hypertrophied, including 2 cases in whom scars were present, presumably from previously caseating cervical glands. Of the 79 children in whom enlarged glands were found, 60 per cent. had tuberculosis.

Enlarged lymph nodes were present in three-fifths of all those children who reacted to tuberculin, and in our subjects who showed definite pulmonary symptoms and physical signs a slightly larger proportion of those who had enlarged nodes in addition reacted to tuberculin than did those which had no such enlargement. On the other hand, of those children who had symptoms but no physical signs, only two-thirds of those who also had enlarged nodes reacted to tuberculin, while of such children who did not have enlarged nodes all reacted.

In addition we noted that hypertrophied lymph nodes were present in the same proportion of those children who had permanent physical signs and of those who did not, and that they were present in only 40 per cent. of our subjects who showed the usual typical physical signs of tuberculosis in the lungs.

7. *Hypertrophied Tonsils and Adenoids*—These were present in 65 of our cases; 31 of these children, or 47 per cent., were considered tuberculous.

They were present in only 43 per cent. of the children reacting to tuberculin, in 35 per cent. of those who had physical signs in the lungs, and in only 20 per cent. of those who had typical pulmonary signs. Of the children who gave a history of cough, 7 per cent. more of those who did not have enlarged tonsils reacted than of those with them. These results were contrary to our expectations and do not accord with the findings of several other observers. They are, of course, at decided variance with general opinion on this subject.

Conclusions.

1. In the children of tuberculous parents, who live in close association with such parents, a large proportion (in our series 51 per cent.) become infected with tuberculosis.

2. The earliest manifestations of such tuberculosis are not found in the superficial glands or in the bones and joints, but in the lungs.

3. The physical signs of these early pulmonary lesions, in children under 10 years of age, are very rarely those usually found in adults, but consist more often in the presence of persistent fine râles just without the mid-clavicular line in the fifth and sixth intercostal spaces. In other cases in which sibilant râles are present in varying portions of the chest, the diagnosis is doubtful, but they should be regarded with suspicion.

4. The tuberculin tests furnish the most reliable means of diagnosis of tuberculosis in children. Of these we regard the hypodermic test in doses up to 5 mg. as positively diagnostic. Of the local tests the cutaneous is more reliable in children than the ophthalmic and presents none of its possible dangers. Moreover, it has in our hands been fully corroborated by the hypodermic test, and in consequence we regard it as a reliable and safe means of diagnosis of tuberculosis in children.

5. Examination of the sputum, as usually practiced, is of almost no aid in the diagnosis of early pulmonary tuberculosis in children. As a routine procedure it is not very feasible in dispensary practice.

6. Malnutrition is sometimes the only appreciable evidence of tuberculosis in children.

7. The presence of hypertrophied tonsils and adenoid growths in any child does not appear to incline the balance in a suspected case toward a positive diagnosis of tuberculosis. In view, however, of the varying opinions held on this subject, further investigations along the lines of the bacteriology and pathology of this subject should be made.

8. In our cases the evidence that the enlargement of the cervical lymph nodes is of aid as a determining factor in arriving at a diagnosis of tuberculosis in children is not conclusive.

THE TUBERCULIN TREATMENT OF PULMONARY TUBERCULOSIS IN OFFICE AND DISPENSARY PRACTICE.*

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Present medical opinion in regard to the use of tuberculin may be roughly divided into three categories.

In the first are those who are still influenced by the early antipathy to tuberculin, caused by its misuse and fostered by the denunciation of Virchow. These men believe tuberculin to be too injurious an agent for medical use.

In the second group are those who see in its striking and easily demonstrated effects on the tuberculous individual a short cut to diagnosis and treatment which will spare the necessity for the more laborious and painstaking methods.

And lastly, we have those who believe strongly in the value of tuberculin, but have come to realize its limitations, so that it is welcomed simply as one more valuable aid to be used in careful conjunction with all other known and accepted methods for the diagnosis and treatment of tuberculosis.

Almost without exception, those who have had extensive practical experience with tuberculin for treatment are now included in this last category. In consequence, tuberculin is now being used very widely, but the majority of reports have come from sanatoria, so that the value of this method of treatment in office and dispensary practice is not yet generally appreciated.

Undoubtedly, it is preferable to have cases of pulmonary tuberculosis under strict supervision, and it is advisable for any one to gain his first experience with tuberculin from patients in institutions where they can be carefully watched and studied. There are, however, no insurmountable obstacles to the employment of tuberculin therapy in the class of ambulatory patients here under consideration. This class constitutes by far the vast majority of all cases of tuberculosis, and consequently any method of treatment which can be advantageously applied to these cases has immediately a very wide sphere of usefulness.

Already good results have been reported with dispensary patients, among others, notably by Hammer, Denys, and Raw in Europe, and in this country by Hawes and Floyd, in Boston, and Hamman and Wolman, in Baltimore. Their experience agrees with our own in New York, that the results of tuberculin treatment are most encouraging, and that they can be obtained in a dispensary as well as in a sanitorium.

Rationale of Tuberculin Therapeutics—It has been conclusively demonstrated that tuberculin does not produce an immunity to tuberculosis either clinically or experimentally. The claim for its specific action in tuberculosis is based upon the following clinical phenomena:

1. It produces a specific hyperæmia at the site of the lesion which has distinct therapeutic value by stimulating both local resistance and the production of antibodies.

2. It causes a specific response in some of the vital reactions of the body which are closely associated with true immunity, *e. g.*, opsonins, agglutinins, precipitins.

3. It establishes a toxine tolerance which is also, perhaps, a real toxic immunity.

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Upon the first phenomenon of local reaction, Koch based his original ideas of treatment but by large dosage carried it to such an extreme that great harm resulted and the method soon fell into deserved disrepute. With the small doses now given, this factor of slight local reaction is undoubtedly very important.

Wright, in his work, has made use of the second phenomenon, *i. e.*, change in the opsonic index as a basis of treatment. In pulmonary tuberculosis this has proved unreliable and unsatisfactory.

The third phenomenon of toxine tolerance is the one upon which the so-called "clinical method" of treatment has been based, and it is this method with minor variations which is at present generally employed.

The Method of Toxine Tolerance—For many years a few far sighted clinicians have recognized that in Koch's discredited cure there lurked a valuable adjunct to the treatment of tuberculosis. The careful clinical observations of these men, Trudeau, Möller, Petruschky, Loewenstein, Denys, Spengler, and others, gradually developed what may be designated the method of tuberculin tolerance.

This method may be defined as the gradual habituation of a patient to the hypodermic administration of increasing doses of tuberculin, beginning with an amount easily tolerated and proceeding over a long period of time to large doses, without the production of any marked constitutional reactions.

Opinions differ concerning minor features of this method, as to the size of the beginning and final doses, the rapidity of increase, the duration and continuity of treatment, the significance of mild reactions, etc., but in the essential principles there is now a general agreement, and in the other details observers are gradually coming nearer to meeting upon common ground.

Selection of Tuberculin—The active principle, the method of action, and the efficacy of all the various preparations of tuberculin are practically the same. Koch's old tuberculin, (O. T.), is the standard and is probably quite as efficient as any of its modifications. Bacillus emulsion, (B. E.) and Koch's new tuberculin, (T. R.) are theoretically better vaccines. They are, however, apt to produce unexpected reactions and clinically produce no better results than the filtered preparations. *Bouillon filtré*, (B. F.), theoretically is preferable because unaltered by heat. Practically its only advantage appears to be its somewhat easier tolerance in excessively sensitive individuals. The assertion that bovine tuberculin is preferable in many cases, rests upon insufficient evidence, and the fact that the human type of bacillus is recovered from almost all cases of pulmonary tuberculosis in adults, deprives the arguments raised in its favor of much weight in the cases which are here considered.

There are many other modifications of tuberculin, none of which have become widely used, nor have they shown any superiority to the few already mentioned.

Selection of Cases—Tuberculin should as a rule be used for treatment in pulmonary tuberculosis only in such patients who have no rise in temperature and are in good physical condition.

Inasmuch as success depends upon a reaction of the tissues of the body to the stimulus of the toxine introduced, if these tissues are not capable of such response, as in very acutely active or very far advanced cases, harm rather than good is usually the result.

In certain selected cases under strict supervision and after a large experience have been acquired, febrile cases may sometimes be treated to advantage, but they are exceptional. Such patients should of course never be treated in office or dispensary practice.

Incipient and moderately advanced cases of course do better under this than any other known method of treatment; nevertheless, the most strikingly favorable results are obtained in cases of long standing where the patients have drifted along into chronic invalidism with perhaps only occasional evidences of active symptoms but with a slowly progressive extension of the lesion and increasing constitutional impairment. The cases with which I have had personally to do are largely of this class.

Incipient cases I have always sent to sanatoria or health resorts if possible, and I have never felt justified in advising any patients in early, favorable cases for whom sanatorium treatment was available to remain in New York in order that they might receive the tuberculin treatment. When patients in such incipient cases do stay in town for one reason or another, they of course do better under the tuberculin than do the more advanced cases under similar conditions. On the other hand, it is interesting to note that not a few of my patients have been those who have tried climatic treatment for years without arrest of their disease, and having come home to gradually drift downward to the apparently inevitable final result, have made remarkable improvement under the use of tuberculin, and in many cases have been able to resume their ordinary occupations.

Accessory Methods of Treatment—The ordinary methods of the hygienic dietetic treatment of the disease must never be neglected in cases treated with tuberculin. In dispensary and office practice in a large city this is by no means easy, and this portion of the treatment is very seldom as satisfactory or complete as could be desired. For this reason, however, the effect of the tuberculin as distinguished from that of the environment can be more clearly determined than is possible in sanatoria.

Almost invariably it is my custom to give each patient before beginning the tuberculin a preliminary course of absolute rest, combined with as much good air and good food as is feasible. Sometimes this has been in the country near New York, but usually in the city itself. This preliminary rest is important in order to enhance the general resisting powers of the patient, and thus favor a proper response to the process of active immunization.

During the earlier part of the treatment also, rest is still a large factor, but gradually more exercise is allowed, according to the individual indications, and not a few of my patients have worked regularly at their usual occupations during the greater portion of the course. Any unusual exertion or strain is prohibited for twenty-four hours after each injection, but absolute rest at these times is not essential.

Private patients have usually lived in the suburbs, where conditions are more conducive to the open air life, and have come in for treatment twice a week. No harm has resulted from these trips, and on account of their better surroundings these patients have, as a rule, done better than those in the dispensary. In a few instances local physicians have given the injections under my general supervision, the patient reporting to me only once in every two weeks or thereabouts.

Some private patients and all of those in the dispensary have lived in New York continuously. For the latter, the visiting nurse, aided when necessary by charitable societies, has done as much as possible to rearrange the tenement home in the best interests of the patient. Nothing more has been done, however, for the tuberculin treated patients than for the other patients under the care of the dispensary.

The day camp has been of considerable benefit by affording favorable conditions during the day for not a few of the dispensary patients. A few of them have also attended the night camp, thus having opportunity for sleeping in the open air.

Very few drugs have been given, and these only occasionally for the relief of special symptoms.

Technique—The injections have been given as a general rule twice weekly until high doses are reached, when the interval is lengthened. They are given subcutaneously in the interscapular region with the ordinary precautions for a hypodermic injection. No cases of infection have occurred.

The dilutions are made with a one-fourth per cent. carbolic solutions and are renewed at least every ten days. It is a distinct advantage for the administrator to make his own dilutions. It is a comparatively simple procedure, and familiarity with it gives one a better knowledge of the agent that he is using. It also fixes responsibility for exact accuracy and avoids needless delay.

The patient records his temperature and pulse three times daily and is warned of the symptoms of reaction for which he must watch. In some cases tuberculin record books have been used, but often the catalogue of possibilities spread before him has rendered the patient too introspective, and in dispensary patients few have the necessary intelligence for accurate observation, so that the use of these books has been the exception rather than the rule.

In these cases even more care must be taken to note the effects of the previous injection than in cases under closer supervision. Careful questioning of the patient, together with the temperature record and examination of the site of injection, have given us satisfactory information, but in case of doubt no chances of reaction are ever taken, and the dosage is either repeated or omitted altogether.

Dosage—The clinical method of gaining tuberculin tolerance without constitutional reaction is the usual one employed and the only one with which I have had much practical experience.

Two different schemes of dosage are widely employed. The first, advocated by Möller, Löwenstein, and others in Germany, begins with from 0.00001 to 0.0001 gramme of O. T. or B. F. and increases rapidly, often by doubling the dose, very soon reaching high dosage. The second, recommended by Trudeau, Denys and Sahli, begins with from 0.00000001 to 0.0000001 gramme, and proceeds much more slowly by fractional increases on a modified decimal system. For a general scheme, the latter is undoubtedly the better and safer method. Reactions very seldom occur and no harm can be done, while the results are very satisfactory. By the first method reactions occur frequently, and in unskilled hands intolerance to tuberculin can easily result.

Nevertheless, it is our experience that patients who take kindly to this higher and more rapid dosage improve more rapidly and perceptibly than do patients with similar cases by the other method. Moreover, by the lower scheme some patients appear to be unaffected as though the dosage was too far below their degree of tolerance. Consequently, as soon as experience with tuberculin has been gained, advantage results from careful individualization in the dosage for each patient, the object being to keep very close to the limit of tolerance and still not cause reactions.

In a general way, the Trudeau-Denys scheme may be regarded as the lowest to be used, and the Möller-Lowenstein scheme as the highest. Best results are obtained by skillful individual variation of dosage between these two extremes.

The maximum end dose to be attained is also a question of individual requirement. In a general way, 1.0 gramme may be considered the maximum dose ever to be employed, but in many cases this can never be reached, because of tuberculin intolerance. In these cases quite as good clinical results ensue from a very slow progression of dosage up to 10 mg. 1 mg., or even 0.1 mg., as the case may be.

White recommends a method of determining the proper dose for each individual by a determination of the amount of tuberculin required to give a cutaneous reaction by the von Pirquet method. I have had no experience with this method, which is ingenious, but appears open to sources of error from individual variations in the absorption of tuberculin through a skin abrasion.

In using B. E., it has become my custom to reckon the dosage by volume just as is done in the filtered preparations, 1 c.c. of the emulsion being considered equal to 1.0 gramme of O. T. or B. F., and upon this basis the same dosage as that already described for these latter preparations being employed.

The amount of solid substance can, of course, be readily reckoned from this, but I am convinced that the usual beginning dose of from 0.0000001 to 0.000001 gramme of solid substance is much too high and partly accounts for the more frequent reactions caused by this preparation. By the volumetric method the beginning dose is only 0.000000005 gramme of solid substance.

Guides to Dosage—The underlying principle should always be to avoid every constitutional reaction, however slight, to the increasing doses of tuberculin.

Too great emphasis cannot be placed upon the importance of watching closely for slight evidences of intolerance to tuberculin, as shown by malaise, loss of appetite, headache, moderate loss of weight, etc., even when no febrile reaction has been produced.

Increased cough and expectoration, pains in the chest, and even slight hæmoptyses are evidences of a focal reaction in the lungs, and must necessarily be considered carefully. I do not feel, however, that such reactions, if slight, show the same tendency to intolerance as do the slight constitutional reactions, and it has often seemed as though a very slight focal reaction was beneficial. We are here treading, however, on very delicate ground, and the exercise of additional care is necessary in these cases for, of course, any considerable focal reaction is not only undesirable but may even be dangerous.

The local reaction at the point of injection should also be carefully considered, there usually being no disturbance beyond a slight sensitiveness for a few hours. The appearance of local pain, redness, or swelling is an excellent indication of an approach to the limit of tolerance, and should be so considered in estimating the proper progression of dosage.

Patients with any tendency to constitutional reaction are given a rest from the treatment for several days or more, and then either the same dose repeated, or some fraction even as far down as 0.1 of the preceding dose given, depending entirely upon the severity and the duration of the reaction that has been produced.

In a general way a mild constitutional reaction protracted over several days is more serious than a sharper reaction, which quickly disappears. A new injection should never be given until all signs of reaction have been absent for several days.

The opsonic index as a guide to dosage, as advocated by Wright, is largely used in England. This is the most scientific guide to dosage that has been proposed, but practically it has proved unreliable, especially so in pulmonary tuberculosis, and its use has been generally discarded. Other proposed guides, such as the agglutination test and the differential neutrophile blood count of Arneth have not proved to be of value.

Duration of Treatment—No results of any permanent value can be obtained unless the tuberculin is continued for a long time, at least six months. Very little beneficial effect is noted before two or three months, and this is not permanent unless followed up. The desirable length of treatment will probably average eight or nine months and not a few individual cases require a year or even eighteen months. This is

a great disadvantage as it is always difficult and often impossible to keep patients under regular observation so long. This is particularly true in the patients who do well and consequently do not realize the importance of further treatment, and in the dispensary cases, even though the visiting nurses do their best to follow up the patients in their homes.

Repeated Courses—In many cases, especially those of the chronic advanced type, more than one course of tuberculin treatment is advisable. The secondary courses are shorter than the first, and the doses increased much more rapidly. The necessity for a second course is determined largely by the clinical symptoms. A return of the evidences of toxæmia is the most valuable indication. A return of response to the cutaneous test may also be of value when considered in conjunction with the clinical evidence.

Results—The chief beneficial results from the use of tuberculin are the disappearance of toxic symptoms and the greater permanency of the regained good health. There is also some evidence to show that tubercle bacilli disappear from the sputum more frequently in tuberculin treated cases, but the direct influence upon the pulmonary lesions as indicated by physical signs, is not striking, indeed is often not appreciable. On advanced cases the improved conditions are most marked, and to note the frequent return to normal methods of living in patients who have been chronic invalids for years is a most gratifying experience. The stability of results is especially striking in dispensary patients. In spite of untoward environment, relapses are comparatively infrequent after tuberculin treatment and the ability to withstand the stress and strain of life is often very surprising.

In a chronic disease dependent upon so many varying factors, the value of statistics is open to question. Nevertheless, enough statistical evidence concerning tuberculin has now accumulated to lend substantial support to clinical impressions of the value of this method of treatment in out-patient practice.

Denys, in 442 cases of all stages, the majority of which were extramural patients, reports an apparent cure in fifty-six per cent. and an improvement in seventy-one per cent.

Hammer, without giving any figures, states that he uses tuberculin for treatment at the Heidelberg Medical Policlinic on practically all patients, most of whom belong to the laboring classes, and that his results are excellent and advises its general use in dispensary practice.

Hawes and Floyd, in forty-six cases of pulmonary tuberculosis treated in the dispensary, report thirty-two arrested, seven improved, and seven unimproved. Compared with patients under similar conditions not treated with tuberculin, they state the difference in results obtained were that the tuberculin treated cases after arrest did not relapse as soon as the untreated cases.

Hamman and Wolman, in fifty-seven dispensary cases of pulmonary tuberculosis of all stages treated with tuberculin at least ninety days, found ten patients apparently cured, sixteen arrested, twelve improved and nineteen progressive.

In my own experience in New York, out of 212 cases treated with tuberculin in office and dispensary practice, only 70 patients continued under treatment ninety days or more. In these seventy cases the following results were obtained: Apparently cured, sixteen, 22.8 per cent.; arrested, twenty, 28.6 per cent; improved, sixteen, 22.8 per cent.; progressive, eighteen, 25.7 per cent.

Present Condition—Well in active life, 28, 40 per cent.; feel well, still under treatment, 13, 18.5 per cent.; total, 58.5 per cent.; not doing well, 6, 8.5 per cent.; dead, 10, 14.3 per cent.; untraced, 13, 18.5 per cent.

Stage of Disease—Incipient, 9, 12.8 per cent.; moderately advanced, 42, 60 per cent.; far advanced, 19, 27.2 per cent.; 87.2 per cent.

Duration of Treatment—Five months at least, 49; nine months at least, 15; twelve months at least, 6. Patients working while under treatment, eight.

Relation of Stage to Results:

	Apparently cured.	Arrested.	Improved.	Progressive.	Total.
Incipient	7	1	1	0	9
Moderately advanced	8	16	12	6	42
Far advanced	1	3	3	12	19
	16	20	16	18	70

Particular attention is called to the fact that although 87.2 per cent. were advanced or far advanced cases, 51.4 per cent. were apparently cured or arrested. That eight patients worked regularly during the course of treatment and that although these patients here reported have been treated over a period of five years, yet at the present time 58.5 per cent. are known to be well and forty per cent. having finished their treatment are now well and leading active lives.

Summary—The present position of tuberculin therapy may be summarized as follows:

1. Tuberculin is a valuable addition to our means of treating pulmonary tuberculosis, its effects being best evidenced by a greater permanence of good results, a larger proportion of cases which lose bacilli from their sputum, and the relief from toxic symptoms, especially in chronic advanced cases.
2. Tuberculin can do no harm when given carefully in proper dosage.
3. No one of the more ordinary preparations of tuberculin possesses any material advantage over the others.
4. The so called clinical method is the most practicable guide for the administration of tuberculin in pulmonary tuberculosis, and the aim should be to produce no general reactions.
5. The time element in treatment is more important than the absolute dosage, the latter varying with every case and the former being never less than six and often more than eighteen months.
6. With unimportant modification this method of treatment is quite as applicable to dispensary and office patients as to those in sanatoria.

THE USE OF DAY CAMPS AND NIGHT CAMPS IN THE HOME TREATMENT OF TUBERCULOSIS IN NEW YORK CITY.*

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The day camp is a comparatively recent factor in the home treatment of tuberculosis in New York City. The night camp was its logical sequel. The separate clinic, devoted exclusively to the treatment of tuberculosis, was inaugurated in New York sixteen years ago, but the establishment of such clinics did not become general among the city dispensaries for ten years afterwards, and the day camp was not a factor in the tuberculosis crusade until the summer of 1907, when the Relief Committee of the Charity Organization Society, the forerunner of the Association of Tuberculosis Clinics, first utilized an old ferryboat for this purpose. The "Southfield," condemned for active service, was secured from the City, equipped with the mere essentials for such use, and maintained as a floating day camp, tied up to a wharf at the foot of West Sixteenth street, for the summer months.

This venture proved so successful that the "Southfield" was secured the following year by the Bellevue Clinic, stationed at a wharf in front of Bellevue Hospital, and has been in commission there, summer and winter, ever since. The liberal use of white enamel paint, and the addition of running water, shower baths, sanitary plumbing and steam heat have transformed the old hulk into a veritable floating hospital admirably adapted to the purpose it now serves.

This transformation of a condemned municipal ferryboat—unfit for active service and consigned to rot away at Staten Island, a useless and unsightly mass of old timber and rusting machinery—into an open air camp for the treatment of tuberculosis was an idea speedily imitated by two more of the city clinics, the Gouverneur and Presbyterian Hospital Clinics. During the summer of 1908, two other old ferryboats, the "Westfield" and the "Middletown," were rescued from the junk heap, with the consent and assistance of the City authorities, and were towed up from Staten Island to their present headquarters on the East River, at the foot of Jackson street and of Ninety-first street respectively, where they were made fit for their present service.

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The Presbyterian boat camp was made possible through the generosity of Mrs. J. Borden Harriman, Chairman of the Women's Auxiliary of the Presbyterian Tuberculosis Clinic, who sustained the expense of its renovation and equipment. It is by far the most elaborate and ornamental of the remodeled ferryboats, and boasts an average daily attendance of seventy-nine. Within the past year, the Presbyterian Clinic has relinquished the control of this camp, which is now maintained by the Board of Health.

The Bellevue boat has also been made more ornamental, as well as more suitable for its purpose, at a considerable expenditure of money. It is now equipped with every necessity for use both day and night, at all seasons of the year.

The Gouverneur boat alone has been altered only so far as to make it habitable, and with the least possible expenditure. With its exterior unpainted and its rusty smokestack the old "Westfield," as one approaches it from the wharf, looks the picture of forlorn and useless dilapidation; but the interior—with its model kitchen, its immaculate dormitory and dining-rooms, its open air school room, and its general air of service with efficiency—makes an altogether different impression.

I speak of the Gouverneur boat with more assurance, and with no intention of drawing a comparison, because I have been associated with the Gouverneur Tuberculosis Clinic since its organization, six and a half years ago, and the camp is one of the by-products of its activity in the Gouverneur district.

The ferryboat "Westfield" and the use of Pier 53, East River, at which it is moored, were secured from the City authorities through the initiative and energy of Mrs. Edward Mandel, the Chairman of the Women's Auxiliary to Gouverneur Clinic. It was opened July 11, 1908, and was conducted until October 25, practically as a private enterprise, and the figures of that early venture will serve as an illustration of how much can be accomplished with limited funds, provided enough enthusiasm and executive ability can be brought to bear on the problem.

During the first season of 1908, the "Westfield" was used as an open-air camp for consumptives for seventy-one consecutive days. In this time ninety-nine patients received the benefit of the treatment, the average daily attendance being twenty-five. During this period, also, the first attempt at a night camp was initiated, nine of the men patients, for whom cots and bedding were provided, being allowed to sleep on the boat. On the closing of the camp in October, necessitated by inadequate facilities for winter weather as well as by the exhaustion of available funds, forty-five patients had improved sufficiently to be able to return to work, and it was possible to send nine others to sanatoria. The remainder continued their regular treatment at the dispensary.

The cost of the undertaking was as follows.

Initial expense of putting boat in condition	$194.53
Nurse—Furnished and paid by the Health Department	175.00
Services, including assistant nurse	240.15
Food and medical supplies	219.96
Car fare and loans to patients	33.80
Office, printing, postage and telephone	28.65
Sundries, including laundry	7.86
Average cost per patient per day	.40½

This, it must be admitted, is reducing the operation of a day camp to its simplest terms. It will be seen that, with the exception of the salary of the head nurse, which was generously assumed by the Health Department, the entire amount was raised and administered by the Women's Auxiliary. It was a large undertaking, splendidly carried through, but the limitation of funds made necessary certain limitations in the work. It was not possible, for example, to provide an adequate noon meal for the patients, and the amount of milk and eggs supplied was necessarily limited. The point was proved, however, that a day camp could be conducted in connection with a large city clinic without an expense out of proportion to the benefit derived from it; and having established that fact, for which she had long contended, Mrs. Mandel gladly relinquished the management of the boat to the City authorities.

The "Westfield" is now under the official management of the Trustees of Bellevue and Allied Hospitals, and with the consequent increase of funds, equipments and facilities we are now able to report these additional figures for the work of the last year (1909):

From May 19, 1909, to January 1, 1910—that is, from the opening of the camp under municipal control up to the beginning of the present year, a period of seven and a half months—331 patients were admitted: 187 men, 81 women, 27 boys, and 36 girls.

During this time there have been discharged from the camp 238 patients: 156 men, 49 women, 17 boys, and 16 girls. There were, therefore, under observation at the camp at the beginning of this year 93 patients: 31 men, 32 women, and 30 children. At the time of their discharge 30 patients were improved and 9 were arrested, 24 were able to return to work, 40 were sent to sanatoria, 5 returned to Europe, 7 were sent to the country, and there were 3 who died. The total attendance of all patients, at both day and night camps, during this time was 14,941. The average daily attendance was 62. A more detailed account of the medical aspect of the work is not within the scope of this paper. As to the cost, I am unable, at present, to give the figures, since our supplies of all kinds are now furnished, on requisition, from Bellevue and Allied Hospitals.

We have now three salaried nurses on the boat—two by day and one at night—as well as a teacher for the school, a clerk, a night orderly, a cook and a scrub woman. The upper deck has been fully equipped for a night camp, with accommodations for thirty men patients. An open-air school for tuberculous children is conducted daily, our teacher being provided by the Board of Education. A hot noon meal is served to all patients, and additional milk and eggs are provided in the morning and afternoon. It is possible now to accommodate not only our own suitable cases, from Gouverneur Clinic, but also those from the two tuberculosis districts adjoining ours, that of the Good Samaritan and the New York Dispensary Clinics.

The routine management of the city camps is similar in all essential particulars. I shall describe that at the Gouverneur camp only because I am more familiar with it. The patients attending day camp are required to report at 9 o'clock in the morning, when their temperature and pulse are taken and recorded by the nurse. Those who have been selected by the physicians as suitable for light work are detailed, in rotation, to do some of the necessary work of the boat. The heavier cleaning and the cooking are done by paid assistants. The majority of the patients are required to rest quietly in their steamer chairs in the open air—the women on the upper, the men on the lower deck—the greater part of the day. Here they may read, or write, or sew, or chat, except during the dinner hour, the serving of morning and afternoon nourishments, and during the "rest hour." Between 1 and 2 o'clock in the afternoon, directly after dinner, absolute silence and rest is enforced, the patients being required to stay quietly in their chairs, all work and conversation forbidden. Many of the smaller children, and some of the older patients, sleep during the rest hour, a habit which we encourage.

The children have regular school hours, somewhat shorter than the ordinary, and are also given selected breathing exercises and calisthenics under the supervision of the physicians. Their school room is the open air.

Strict sanitary rules are enforced with all patients, the penalty of carelessness or disobedience being dismissal from the boat. These rules are displayed on conspicuous placards, printed in English and Yiddish, the latter being our prevailing tongue in the Gouverneur district, and they are also given, on small printed leaflets, to each patient admitted to the camp All patients are required to be familiar with them.

The day patients are dismissed at 5 o'clock, after the afternoon temperature and pulse are recorded. They are weighed, and the weights charted, once a week. We are now making an effort to adapt the dietary to a standard of caloric efficiency, but this is rendered difficult on our boat by the racial prejudices of our patients, the overwhelming majority of whom are Hebrews, to whom some foods of high caloric value, as bacon, are not acceptable. On the Gouverneur boat only Kosher food is served, since the introduction of which practice our attendance has notably increased.

The physicians associated with the work of Gouverneur Clinic visit the boat regularly, four medical rounds, as well as seeing all Gouverneur cases every week at the dispensary.

Many of our night camp patients also attend the day camp, thus living on the boat, under much the same discipline that they would follow at a sanatorium. Several of them are able to work by day. Night camp patients are required to report to the night nurse not later than 9 o'clock. Their morning and evening temperatures are recorded, and they are weighed every week, just as the day patients. They sleep on comfortable and sanitary hospital cots, with clean, fresh bedding—for the care of which they are held responsible—and, though protected from wind and rain, they sleep in the open air. The contrast between the night camp dormitory and the average tenement home, especially on a stifling summer night, is startling; and yet some of the more ignorant of our patients can with difficulty be persuaded to remain. Such is the work of the Gouverneur day and night camps, and the results, the improvement in the condition of the patients—as recorded in symptoms, physical signs, and gains in weight—more than justify the expenditure of time, effort and money.

Before concluding this account of the larger city day camps, mention should be made of the splendid day and night camps maintained by the Vanderbilt Tuberculosis Clinic, on the roof of the Clinic building, and by the Tuberculosis Clinic of the Nose, Throat and Lung Hospital. I am not personally familiar with the details of the work of either, but they are both completely equipped and excellently conducted.

The abandoned ferryboat, with its ample deck room and open cabins, and with its location and outlook, on all the endless variety of river and harbor activities—provides an almost ideal camp for New York clinics; but the expense of adapting such a boat to such a purpose is considerable, at the very least, and can only be justified by the large numbers of patients who can be treated. Obviously, such boat camps are only feasible in large cities with long water fronts and abundant wharfage.

Even in New York, the boat camp cannot wholly, or even very largely, solve our problem. There are a very limited number of such boats, of places to put them, or of clinics to support them. Furthermore, in dealing with smaller and selected groups of patients, as in the tuberculosis classes, the problem of a day camp is a very different one. Such patients cannot, or will not, attend a large city boat camp, and it is often well-nigh impossible, in New York, to secure them outdoor treatment at their homes. It is forbidden by law to use the fire escapes for this purpose—although, in the case of a tuberculous patient, an infringement of the law is sometimes overlooked—and the landlords and neighbors of our patients seem to have a rooted objection to such use of tenement roofs. Dr. Pratt in Boston speaks of the use of back yards as suitable for tents and shacks. Back yards large enough to serve for this purpose are beautifully lacking in most of our New York tenements, and, when present, are preempted by everything from stray cats to the week's wash. It is often only by moving an entire family into light and sunny quarters, and providing a window tent for the patient, that we have been able to solve the problem for some of our class patients at St. George's.

That was our predicament before the establishment of our own day and night camp on the roof of St. George's Deaconess' House. This was made possible, in February, 1909, through the generous co-operation of the Deaconess House Committee, and has been one of the most successful features of our work during the past year. The top floor of the Deaconess House, which communicates with this roof, was originally planned as a miniature hospital floor for convalescent patients. As our tuberculosis class work grew, it was felt that a greater amount of good could be done for a greater number of persons by placing this floor, and its equipment, at the disposal of the class. Our camp therefore consists, in addition to the roof, of a bedroom (used as a dressing room only, since no patients were allowed to sleep indoors), a bath room, private hall, dining room, and diet kitchen. The hall communicates directly with the flat, brick-tiled roof, partly covered by glass and open to the south. The bright colored awnings and window boxes gay with flowers make a cheerful picture on sunny spring days; but, summer or winter, rain or shine, our patients are required to be out.

The routine of the camp is, on its smaller scale, not unlike that already outlined, except that the patients take and record their own temperatures, and are weighed at class every week. The parish nurses and the senior deaconess supervise the daily management of the camp, and members of the committee and one of the class physicians visit regularly. A hot noon meal is sent up from the house kitchen, but separate dishes and utensils are used at the camp and are sterilized by boiling. Milk and eggs are provided morning and afternoon, as well as supper and breakfast for the patients living, night and day, upon the roof. Those attending night camp only receive their breakfast, getting supper at their homes after their day's work.

As the roof space is limited, not more than twelve patients by day and five at night can be accommodated, and only women and children are thus provided for at present. We hope soon to be able to open a similar camp for men on the roof of St. George's Trade School building. At present we have three patients living at the camp day and night—one of whom is kept in bed the entire time, except the afternoon she attends class. One patient comes at night only, a graduate who is now at work. Five others are attending only in the day and go home to sleep.

The average running expenses of the camp amount to about $18 a week, that is, about 28 cents per patient per day.

Since we have been able to conduct this day and night camp at St. George's, we have adopted a new method of discharge for our class members. Heretofore, candidates for discharge—cases arrested or apparently cured—were merely graduated from active membership and allowed to return to work, being required to report every month, at first, for observation; and later, less frequently, if no relapse occurred. Now, our recent "graduates" are required to attend night camp at first upon return-

ing to work—thus getting ten to twelve hours' treatment, at rest out of doors, in the twenty-four—until we deem it safe to restore them wholly to the home environment. It is on this same principle, of making the transition from active treatment to everyday life less abrupt, that we now readmit to the class, after their discharge from sanatoria, those patients whom we have been able to send away.

In conclusion, it seems to me that the day and night camps, as I have seen them in operation, play, in at least three definite ways, a very important part in this crusade against tuberculosis—whether they are conducted in connection with a large clinic, on a large scale, like our ferry-boat camps, or in connection with a church class, on a small scale, like our roof camp at St. George's. First:—They provide the essential of treatment—rest in the open air—under supervision and in a favorable environment. Second:—They provide a place where sanatorium discipline and regime can be taught and maintained. Third:—They provide a place where patients well enough to work by day, or upon their return from sanatoria to home environment, can continue to take the treatment twelve hours out of the twenty-four.

I know of no means at our command which supply these important features of our work better than the day and night camps.

PNEUMOTHORAX: A CLINICAL AND RADIOGRAPHIC STUDY.*

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and

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Historical—Pneumothorax as a clinical or pathological entity was not known to the fathers of medicine. They did not differentiate it from empyema; and it was in the diagnosis of this latter disease that they applied the succession test. This sign—a splashing sound produced in the chest by shaking the patient—was first described in writings credited to Hippocrates, and the procedure is, therefore, frequently called "Hippocratic succussion." For over two thousand years, until the time when Laennec made his classical contribution to the subject of pneumothorax, the true significance of the succussion sign was not understood. The presence of the splashing sound was thought to indicate a moderate amount of pus in the chest, while its absence was interpreted as indicating a chest filled with pus.

As time passed, the importance of this sign was questioned, and it finally came to be considered as having but little value. The reason is apparent when it is remembered how infrequent is the occurrence of hydropneumothorax as compared with empyema, and consequently how seldom the characteristic splashing sound was heard. Thus it was that Morgagni (1) stated that "this symptom neither is nor can be perpetual," and he thought it of little value because of its rarity. With the identification of pneumothorax as a distinct entity, the true meaning of the succussion splash was demonstrated, and its value, as a sign of the presence of fluid associated with air, was established.

That pneumothorax remained unrecognized until the nineteenth century is not at all surprising, for it appears that until 1746 it was believed that air was normally present in the pleural cavity. At that time Haller (2) disproved this view, though a long time elapsed before the correct ideas gained general acceptance.

To judge from the cases reported by Combalusier (3) (1747), Meckel (4) (1759), Ponteau (5) (1783) and Bell (6) (1784) the presence of air in the pleural cavity was at that time recognized as an abnormal condition, and from the proposal of Alexander Monro (7) (1760) and Hewson (8) (1767) to perform thoracentesis for its removal, it is logical to infer that the ill effects of the air in the pleural cavity were understood

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at that date. Still, no clear or definite idea of the disease existed until 1803, when Itard (9) described the condition as found at autopsy and termed the disease pneumothorax. In a crude way he classified the causes of the affection and recognized its relation to tuberculosis. But neither he nor Bayle (10), who also described the autopsy findings in a group of cases, was able to recognize the condition during life.

Laennec (11), however, in 1819, firmly established the disease as a clinical entity. He was perhaps the first to diagnose pneumothorax during life, and he insisted that this could only be done by means of mediate auscultation and the stethoscope. Though his classification is in some respects erroneous, though some of his cases were not true cases of pneumothorax, and though he failed to note some of the accompanying physical changes, his contribution nevertheless stands as one of the milestones of progress in the art of physical diagnosis.

After Laennec's contribution the subject of pneumothorax received considerable attention and discussion. Numerous cases were reported, and the physical signs were investigated and analyzed. According to Emerson, just as Laennec considered mediate auscultation indispensable in the establishment of the diagnosis, so Poirry (12) (1828) maintained the importance of mediate percussion, while Louis (13) (1836) and his pupils laid the greatest emphasis on the clinical history regarding auscultation and percussion as unimportant diagnostic methods. It was not long, however, before these discordant claims were harmonized and the importance and the value of each method duly recognized.

In 1830 Reynaud (14) for the first time collected and reviewed all the literature on the subject and gathered 48 cases. Saussier (15) (1841) wrote an excellent thesis and collected 169 cases. Biach (16) (1880) collected the largest number of cases, 485 from literature and 433 from the records of Vienna hospitals, a total of 918. Drasche (17) (1899) reported and analyzed 198 cases which had come under his personal observation during a period of forty years. Emerson (18) (1903) exhaustively reviewed all the literature upon this subject and reported 48 cases from the Johns Hopkins Hospital. To this latter valuable contribution we desire to express our indebtedness for much of the historical data.

It is surprising to note the little attention this subject of pneumothorax receives in the text books on pediatrics. Pneumothorax is not a rare affection in children. It occurs more frequently than is generally supposed. Holt mentions the condition only in its relation to the pathology of tuberculosis. Koplik discusses it briefly in relation to empyema. Netter and Carr merely comment on its rarity. Rotch, Baginsky, Pfaundler and Schlossman make no mention of it.

It is our purpose to review the subject in a general way, to record clinical and radiographic observations and then to discuss the condition with reference to its occurrence in children.

Classification—Pneumothorax may be produced in any one of three ways: First, by the admission of air into the pleura through a penetrating lesion of the chest wall, the type designated as pneumothorax with an external fistula. Second, by the admission of air into the pleura through a lesion of the lung and visceral pleura or through a communication with a gas-containing organ—pneumothorax with internal fistula. Third, by the bacterial decomposition of a pleural exudate with the formation of gas. When, as in this last variety, there is no communication with the exterior air, a closed pneumothorax is said to exist, in contradistinction to the other variety, in which the air has free egress and ingress, and which is designated as open. The sealing of the fistula either by inflammatory activity or otherwise, may convert a primarily open pneumothorax into a closed one. A peculiar formation of the fistula may permit the air to enter the pleural cavity, but prevent its exist. This is the so-called valvular variety. According to the experiments of Marais and Castlenau (21) and Lister (19), a small wound in the lung is always a valved opening which permits the air to travel in one direction only; that is, from the bronchi to the pleura. This was later emphasized by Bard (20), who states that it is impossible in a normal lung (one free to retract of collapse) to produce a fistula permeable in both directions; that is, one which will permit the egress and ingress of air into the pleura.

Causes—The first variety, according to the classification given, may be produced by stab or gunshot wounds of the chest, by surgical operations, by the accidental admission of air during exploratory puncture and by necrosis of ribs or axillary cellulitis, and, finally, in consequence of the perforation of the chest wall, by a purulent effusion, the so-called "empyema necessitatis." It was recognized early in the study of this condition that not all perforating wounds of the chest will produce pneumothorax, and in Biach's (16) statistics 21 cases with such wounds are cited in which pneumothorax did not result.

The second variety may result from the rupture into the pleural cavity of a tuberculous, purulent or gangrenous focus in the lung, from perforation of a bronchiectatic cavity, or an emphysematous vesicle or from the laceration of the lungs by fractured ribs. It may be produced by compression of, or severe trauma to the chest without evidence of external wound or fracture. Vigorous and prolonged attempts at artificial respiration may give rise to pneumothorax and subcutaneous emphysema. Any cause, in fact, which produces increased intrapulmonary pressure may result in pneumothorax. Thus it has been caused by the severe coughing paroxysms of pertussis and by the straining of persistent vomiting. It has resulted from the perforation of a foreign body in the bronchus. Ulcerative and suppurative processes in the adjacent organs, liver, stomach, esophagus or intestine may perforate into the pleural cavity.

There is a variety of pneumothorax which has been called "spontaneous" because it occurs in apparently normal individuals without evident cause. In these cases the pneumothorax is rarely fatal. Many observers, among them West (22), deny that the lungs are really normal in such cases and believe that the condition is due either to a latent tuberculosis or to the rupture of emphysematous alveoli. The cases which follow slight exertion, or occur without apparent cause, indicate that in some individuals the lungs, because of certain structural pecularities, may be susceptible to rupture. Thus in a case reported by Grenier (98) the pneumothorax recurred three times, in each instance without apparent cause.

Mechanics—The changes produced in the pleural cavity by the entrance of air, the resulting disturbance in the mechanics of respiration, the position and behavior of the lung under the unusual condition and the modus of the restitution to normal, are some of the phases of pneumothorax which have been the subject of much investigation and controversy. These questions are still in many respects unsettled. The conflicting observations recorded by various investigators make it difficult to arrive at any correct conclusions. The lungs may be considered as two hollow, elastic and distensible structures communicating freely with the exterior and suspended within a closed and rigid chamber—the thorax. Each lung is enveloped by a serous membrane, the pleura, which is continuous over the inner surface of the chest. In the normal state the visceral and parietal layers are in contact during expiration and inspiration, so that the pleural cavity, as such, may be said not to exist. Because of its free communication with the exterior, the pressure of the air within the lungs varies but slightly from that of the atmosphere. It is, however, exactly that of the atmosphere only at the end of quiet inspiration and expiration. During the act of inspiration, as the capacity of the thorax is increased, the lungs by virtue of their elasticity, are distended and the intrapulmonary pressure falls. An inrush of air through the trachea takes place until the atmospheric pressure is re-established. During the expiration, because of the collapse of the chest and the recoil of the lung, the intrapulmonary pressure is slightly increased over that of the atmosphere, and air escapes. Even during the most forcible expiration, however, the elastic tension of the lung is not satisfied; it is still on the stretch. Between the pleural layers there is a pressure less than that of the atmosphere which is referred to as a negative pressure. This negative pressure varies during the respiratory phases and is greatest at the end of inspiration. It has been estimated by Aaron (23) as varying from minus 4.64 mms. Hg. at the end of quiet inspiration to minus 3.02 at the end of expiration.

The forces concerned in the maintenance of the lung in its normal position may be divided into two classes: Those acting from without, which may be styled extrinsic, and those due to properties inherent in the lung tissue itself, which may be called intrinsic. The extrinsic forces consist of, first, the pressure of the atmosphere on the exterior of the chest; second, the pressure of the air within the lungs (intrapulmonary) which, with the variations noted, is that of the atmosphere; and third, the tension which exists between the pleural layers (intrapleural negative pressure). The intrinsic forces consist of, first, the elasticity of the lung, which constantly tends to diminish the tension under which its structure has been placed; and second, the tonus of the lung, due to its bronchi, muscular and vascular tissue, which maintains the definite structure and shape of the organ.

When air is admitted between the pleural layers, the negative intrapleural pressure is diminished; that is to say, it approximates the atmospheric. The lung may now satisfy its inherent tendency to shrink. But under certain circumstances there is not only no shrinkage, but there may be an actual protrusion of the lung through the wound in the chest wall, constituting a hernia. There are evidently conservative forces which counteract the tendency of the lung to retract. The older writers sought to explain this non-collapse by assuming that a state of cohesion existed between the

pleural layers. The resistance encountered when an attempt is made to inject air or fluid into the pleura seemed to give force to this idea. Dolbeau and Smith (24) compared this cohesion to that which exists between two opposed wet plates of glass. West (22) believed in this cohesive force and estimated it as being equal to the pressure of 12.5 mms. Hg. But other and later investigators [Northrup (25) and Emerson (18)] have by experiments on animals produced evidence against this cohesion. They have also sought to prove that even the smallest opening of the pleura invariably results in the immediate and complete collapse of the lung, and that under these circumstances the lung takes no part in respiration while the pleural wound is patent. The experiments of others [Hellin (26) and Reinboth (27)] give results which are at variance with these, and demonstrate, on the contrary, that the lungs of animals do not collapse perfectly, even when the pleural opening is the diameter of the trachea, and that the lungs functionate, in the presence of air, in the pleural cavity.

Without attempting to reconcile these antithetical observations, we would insist that it is necessary to be extremely cautious, in the application of the results of animal experimentation in pneumodynamics, to conditions obtaining in human beings; this for several reasons: First, because the anatomical formation of the pleura is different in animals. In the dog, for instance, there is often a communication between the two pleural cavities just above the tendinous centre of the diaphragm, so that nearly every pneumothorax is really bilateral; second, the intrapleural tension is greater in animals; third, the mediastinum is more freely movable in animals. Sehrwald (28) has shown how the mobility of this structure will affect the condition of both the sound and the affected lung; fourthly, the position of the animal influences the activity of the lung in the affected thorax, and Reinboth (27) has furthermore proven that even in the presence of a large opening in the chest wall, if the animal be so placed that the perforation is lowest, the lung will continue to functionate.

These factors undoubtedly influence the experimental results. In their application to human beings, such results should not be permitted to outweigh the information gained by clinical studies. For whatever the experiments on animals may show to the contrary, the following observations remain indisputable, namely, that in human beings pneumothorax does not always result when a communication is established between the pleura and the outside air, that complete collapse of the lung does not usually follow the admission of air into the pleural cavity, and that finally even when pneumothorax is present the lung in the affected cavity usually continues to functionate to a greater or less extent.

In the explanation of the non-collapse of the lung, it is necessary to take into account besides the factors which influence its position (the extrinsic and intrinsic forces), the power of vicarious distention of its alveoli which the lung tissue may exhibit in response to an afferent impulse. The influence also of the size of the pleural wound is important. The integrity of the lung, however, is of greater consequence as affecting the admission of air into the pleural cavity than is the integrity of the chest wall.

When the wound of the pleura is small, that is to say, less than the diameter of the main bronchus to the lung, the tendency of the lung to collapse is counteracted by the compensatory dilatation of parenchyma, in the immediate vicinity of that portion subjected to the stress of the atmospheric pressure. This increase of the pulmonary volume, associated as it is with increased intrapulmonary tension due to increased respiratory activity, is sufficient not only to maintain the approximation of the pleural layers, but when there is added the expiratory pressure from the sound lung, an actual protrusion of the lung tissue into the parietal wound may take place. One condition, however, must be present in order that this may transpire, and that is, the lung must be uninjured and not diseased.

When the opening into the parietal pleura is a large one, air enters the cavity with each inspiration, and the lung shrinks to a corresponding degree. It does not, however, collapse to the same degree as if the wound were in its own tissue. Redistention takes place as soon as the parietal opening becomes smaller through the agency of the same forces as mentioned above, except that the expiratory pressure from the sound lung plays a more important part. The lung continues to take an active part in respiration, but its movement differs from that of the sound lung; that is, it expands with expiration and collapses with inspiration. As the fistula closes the type of respiration changes, and when the size of the opening becomes less than that of the bronchus the normal type again prevails.

When the lung and pulmonary pleura are injured and there results a pneumothorax with internal fistula, the degree of lung retraction will depend upon the size and form of the perforation, on the size and condition of the bronchus leading to the affected parenchyma and on the condition of the lung. Cases are on record in which

perforation of normal lungs did not result in pneumothorax. As a rule, however, despite evidences of reparation, as shown by localized atelectasis by the dilatation of the adjoining parenchyma and by the increased expansion, the air nevertheless escapes into the pleura. As has been pointed out previously, because of the localized atelectasis, the fistula permits the air to enter into the pleura, but prevents its egress, and thus the negative pressure of the pleura is rapidly lowered or changed to a positive

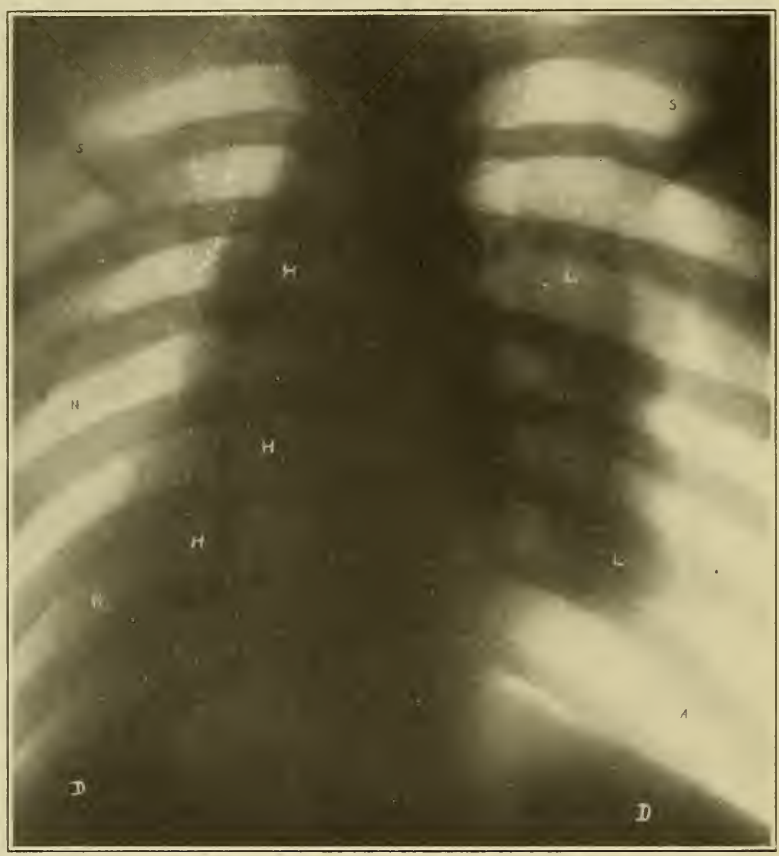

Fig. 1—Pneumothorax—right.

(L) Collapsed lung lying about its root.
(A) Pleural cavity containing air—brilliantly illuminated.
(H) Heart displaced to the left.
(N) Normal lung.
(D) Diaphragm. Note its sharp outline on the right side indicating immobility.
(S) Scapula. Note the difference in density of the ribs' shadows of the right and left chests.

one. It is this positive pressure which indirectly gives rise to the oppressive symptoms, but which at the same time effectually aids in the closure of the fistula and thus initiates the reparative process. If, however, because of disease of the lung or the presence of pleural adhesions, the collapse of the lung is prevented, or if the situation of the wound be such as to expose a bronchial opening, then the exit and entrance of air into the pleural cavity is free and restitution to the normal is delayed.

Effect on Lungs—The air entering the pleura may first be confined by adhesions to a particular part of the chest, and only later occupy the entire cavity. This frequently occurs in pneumothorax due to rupture of a tuberculous lung. As the air enters, the lung collapses as a

whole toward its root, the force of the positive pressure acting upon every part of the periphery and compressing the lung toward this point. Garland (29), from observations upon dead dogs, claims that the base of the lung retracts first, and only after this part ascends for some distance do the other parts collapse. Experimental pneumothorax, as studied with the Roentgen ray, shows that in the living animal the air rapidly diffuses from its point of entry over the entire pleural cavity, and that this primary retraction of the base does not take place, but that every part collapses simultaneously. The position of a collapsed lung in a pleural cavity free from adhesions is always at its root. From this site, if the perforation is small, the lung may be observed to expand from its shrunken condition to take part in the respiratory movements. When, however, the perforation is large and the lung is the seat of disease, the collapse of the lung is usually total and the lung lies against the spinal column as a shrunken mass. Adhesions may permit only part of the lung to collapse, and

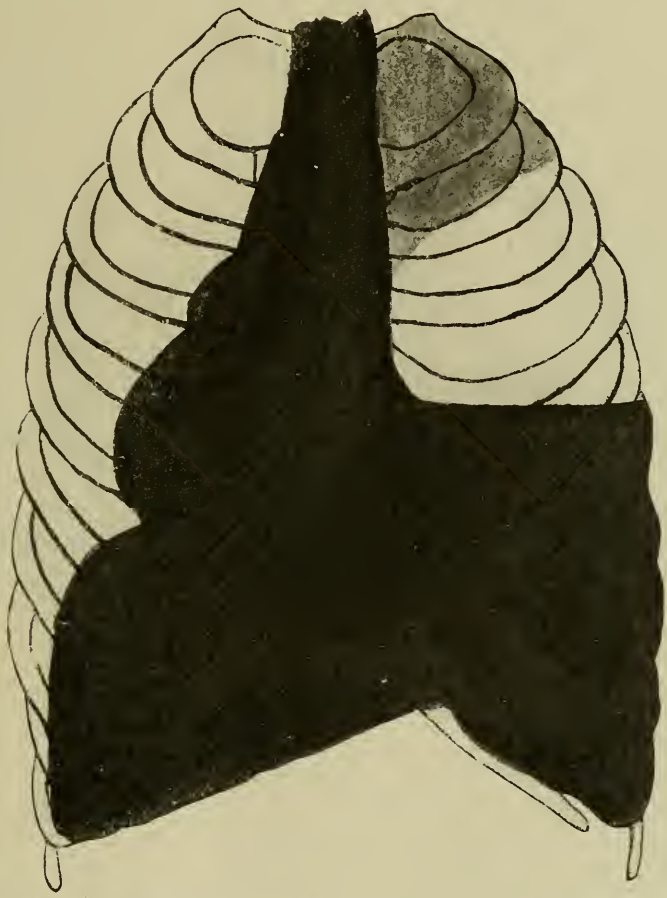

Fig. 2—Diagram of pneumohydrothorax, as shown by Roentgenoscopy. Right side. Upright position. Ventrodorsal view. The three zones are shown. The shaded upper corresponding to the compressed and collapsed lung; the bright middle indicating the air; and the dark lower indicating fluid. This shadow merges with that of the liver below. Heart displaced to the left. The perfectly horizontal line of the upper level of the fluid is shown.

examination with the Roentgen ray of a recent case will show that during respiratory movements the adherent area expands with inspiration, following the pull of the chest, and shrinks with expiration; it is only with forced expiration, however, that the collapsed portion dilates to any extent. With the healing and closure of the fistula, the affected lobe begins to follow the movements of the chest.

Effect on Diaphragm—The diaphragm is depressed to a varying degree. Its dome is flattened and its movements are inhibited In many cases the tone is entirely lost and the diaphragm passively follows the pressure changes in the abdominal cavity, rising with inspiration and sinking with expiration. In cases where massive collapse of the lung persists for some time, the diaphragm may so entirely lose its tone as to sag into the peritoneal cavity. The limitation of the motion of the diaphragm in pneumothorax, as well as in incipient tuberculosis, is not due to any intrinsic affection of this part, but entirely to the loss of the supporting power of the lungs. The loss of tone of the diaphragm results in bulging of the lower chest and widening of the intercostal spaces. This distension is no indication of increased pressure within the pleural cavity, but simply an index of the extent of the paresis of the diaphragm and the intercostal muscles.

Effect on Heart—The mediastinum and its contents may be considered as a movable body, whose position depends upon the surrounding forces. Any change in the intrapulmonary or intrapleural pressure will disturb the equilibrium and affect its position. When the normal negative pressure is lowered by the admission of air, the heart and great vessels will be displaced in the direction of least resistance, and will thus be pushed away from the affected side. The displacement is greater in children than in adults. The displacement is also greater when the left pleural cavity is involved. In these cases, the heart within the right thorax, the distorted aorta and the stretched blood vessels makes a very striking fluoroscopic picture. The position of the heart serves as the best index of the amount of air in the pleural cavity. Recovery can only be considered complete when restitution of this displaced viscus has taken place.

Hydropneumothorax—A not infrequent complication of simple pneumothorax is the accumulation of fluid within the affected pleura. It has been estimated that but 10 per cent. of all cases are free from this complication. The development of an effusion depends to a great extent upon the condition of the pleura and lung prior to the admission of air. If these organs are the seat of an inflammatory condition, the occurrence of an effusion is to be expected, while pneumothorax in a previously healthy pleura may go on to restitution without effusion. According to West, the fluid is serous, sero-purulent and purulent in an equable division of cases. In children, purulent effusion is a very common occurrence. It is unusual for a serous effusion to change gradually to a purulent one. The organisms in the fluid are usually those associated with the primary disease. In perforating wounds the infecting organism may be introduced from without. In the case of May and Bebhard (30) the infecting organism was the colon bacillus introduced through a stab wound.

When fluid accumulates in a pleural cavity containing air, the physical conditions, as viewed by means of the Roentgen ray, are different from those of simple effusion. In ordinary exudative pleurisy the upper level of the fluid appears concave, rising higher at the sides and more so at the outer than the inner, while a change in the position of the thorax has but little effect on this level. In the presence of air, however, the upper surface is horizontal (Fig. 2); the level changes freely with the position of the thorax, but always remains horizontal. Moreover, the fluid is affected by every movement of the body. Thus the rise and fall of the level corresponding to the respiratory movements, the undulations synchronous with the systole and diastole of the heart, the agitation of its surface when the chest is percussed or during coughing, and the waves produced by the more forcible succussion are all phenomena to be observed with the fluoroscopic screen. When moderate in amount the level of the effusion rises with inspiration and falls with expiration—a reversal of what should normally occur. This paradoxical condition is due to the loss of tone of the diaphragm, whose movements become altogether passive and follow the abdominal pressure changes. In the same way as the abdominal wall moves forward with inspiration, so the diaphragm is pushed upward in that phase. When the fluid is considerable the diaphragm may become inverted and so weighed down that the level of the fluid is not appreciably affected by the respiratory movements.

In the presence of air the upper limit of dullness does not indicate the level of the fluid. The low tone of the note is vitiated by the tympanitic resonance due to the presence of air. It has been stated as axiomatic that in these cases the amount of fluid will be double that indicated by the line of dullness [Skoda (31)]. Thus in a case of Senator's, Weil (32) states that the chest was hyperresonant to the twelfth rib even after 800 c.c. of a medicated solution had been added to the fluid already present. A small amount of effusion cannot be made out by the usual methods of examination. The predominating pathological condition will determine the signs which it is possible to elicit. Thus in the presence of considerable gas even a moderate effusion may escape detection, while a small amount of air associated with much effusion will but rarely be diagnosed. The Roentgen ray examination will render considerable aid in

these cases, for even the least effusion in the costodiaphragmatic sinus may easily be made out either by the fluorescent screen or on the photographic plate. (Fig. 3.)

Subcutaneous Emphysema—Subcutaneous emphysema may be a complication of pneumothorax due to exploratory puncture, incision of the chest wall or trauma with or without evidence of fracture or rib. The emphysema may in some instances appear in the tissues of the neck before the air gives evidence of having entered the pleural cavity. This is brought about by the extravasation of air beneath the temporarily intact visceral pleura. From there the air dissects its way into the mediastinal tissues

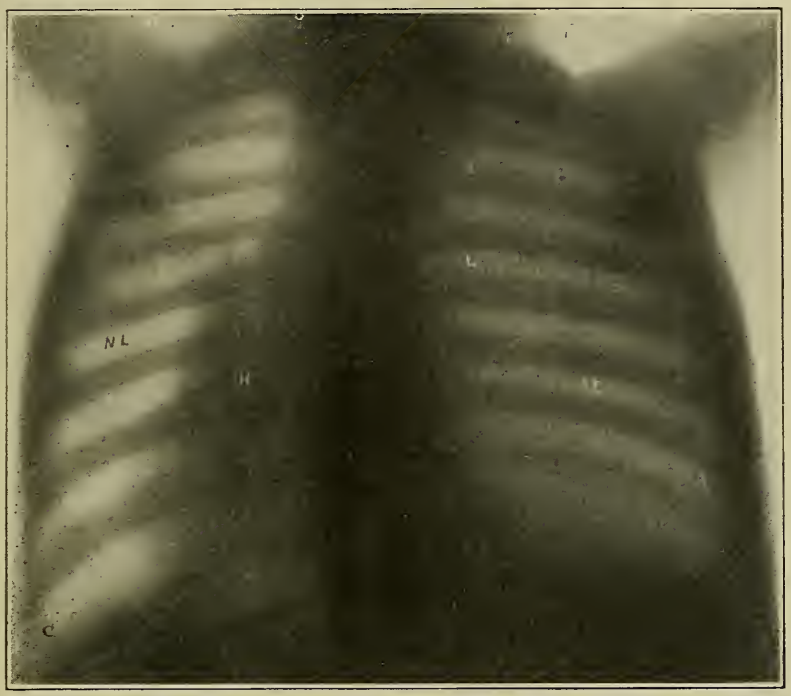

Fig. 3—Pyopneumothorax—right. (Ventrodorsal view.) Recumbent position

(AE) Air and fluid in the right pleural cavity.
(L) Shadow of collapsed lung faintly visible, owing to the superimposed shadow of fluid which, because of the recumbent posture, flows over the posterior wall of the chest while the air rises above it.
(H) Heart displaced to the left.
(NL) Lung on the left side in a state of compensatory emphysema.
(D) Diaphragm.
(C) Costo-diaphragmatic space of right side clearly outlined. Compared with appearance of space on diseased side which contains fluid.

and then into the neck. Later the pressure may cause perforation of the visceral pleura. Such were the events in a case reported by Steffen (79) resulting from the fracture of a rib. Before the importance of pneumothorax was recognized, subcutaneous emphyesma interested the early observers, who ascribed the symptoms of the former disease to its complement or complication subcutaneous emphysema. Ambroise Pare (33) (1628) was perhaps the first who recorded observations upon the presence of air in the subcutaneous tissues, resulting from fractured ribs. As a rule, emphysema, when a complication of pneumothorax does not add to the gravity of the case. Perrin (34) directs attention to the fact that subcutaneous emphysema, following puncture of a pneumothorax, may be a serious complication. The emphysema may become general and require incision or a cellulitis may be set up, if a pleurisy be present. The prognosis, however, is not always grave, and 2 cases are reported in which recovery took place. In both, the emphysema was produced accidentally in thoracentesis. The puncture wound acted as a safety valve compensating for the continual accumulation

of air in the pleural cavity, by evacuating it into the cellular tissues, where it was absorbed. In a case reported by Bovaird (40) the chest of a child of three years, with left pneumothorax, was punctured. Subcutaneous emphysema followed, which spread over the entire body. It is interesting to note that the air in the subcutaneous tissues is absorbed more rapidly than in the pleura. It requires from three to seven days for the air to disappear from beneath the skin, while in the chest it may persist for three or four weeks, or even longer.

Composition of Air in Pneumothorax—The chemical composition of the air in the pleural cavity may become changed in consequence of secondary infections or absorption of some of its constituents. The composition of the gas in cases due to the decomposition of the pleural exudate will depend upon the nature of the infecting organism. The most frequent infecting germs are the bacillus coli communis and the bacillus ærogenes capsulatus. In the recorded case in which the development of gas from decomposition of fluid was supposed to have taken place, paracentesis had been performed, and it is not improbable that the organism may have been introduced in this manner.

Absorption of Air—That the pleura possesses the power of absorbing gases has been proven by animal experiments and observations on human beings. J. Davy (35) (1823) was one of the first to experiment with the absorptive power of the pleura. Pure oxygen is absorbed more readily than nitrogen, while CO_2 and O were absorbed at about the same rate as air. The relative quota of CO_2, in the air which enters the pleura, becomes rapidly greater than that of the atmosphere. More CO_2 is also present if there is an accompanying purulent effusion. The absorption is retarded in the presence of any inflammatory condition of the pleura or lungs. The air disappears more rapidly in children than in adults. The rapidity of absorption varies within wide limits, though it is not unusual for it to be completed in from four to eight weeks. Fowler and Godlie (36) state that a quantity of air sufficient to give a tympanitic note over half of the chest completely disappeared in three days. In a case reported by Aron (23) of a man with emphysema, who developed pneumothorax from inhaling hydrochloric acid fumes, the gas was absorbed in four weeks. In some of the reported cases it has, however, taken months and years before absorption was complete.

Pneumothorax as a Therapeutic Measure—Since Houghton's observations (1832) of the apparently favorable influence of pneumothorax upon the progress of pulmonary tuberculosis, this phase of the subject has been a matter of much controversy. Such excellent clinicians as Stokes, Saussier, West and Walshe have failed to observe any distinct definite or lasting improvement. Potain (87) (1888) was the first to recommend the introduction of sterile air after the removal of the exudate. He believed that this immobilized the lung and favored cicatrization and cure. Forlanini (88) (1894) produced pneumothorax in 2 tuberculous cases with nitrogen gas, and claimed satisfactory results. Murphy (89) recommended this procedure in unilateral tubercular involvement.

Pneumothorax in Children—Pneumothorax, though quite a rare disease in children under three years, is not rare in older children. It may occur in the newborn as a result of trauma. Thus Ruge (38) reported the case of an infant who was born asphyxiated. After resuscitation, it cried lustily during the night, but the next morning became cyanotic and died. The autopsy showed left pneumothorax, the pleural cavity also containing a little blood. It was supposed that there had been a rupture of the alveoli, interstitial emphysema, and finally, rupture of the pleura, and that the condition was due to the violent crying, but from similar cases, which have come under our observation, it appears reasonable to suppose that the efforts at resuscitation played an important part in its production.

James (39) refers to a case reported by Money which occurred in a child of three months. Bovaird (40) reported the autopsy record of a case of pneumothorax due to rupture of a small abscess in a child of four months.

Etiology—In the order of their frequency, the causes of pneumothorax may be stated as follows: Tuberculosis, gangrene, trauma, empyema, foreign bodies and abscess. Pneumothorax frequently complicates those infectious diseases in which bronchopneumonia is a prominent feature, namely, measles, pertussis and diphtheria. It is but rarely due to suppurative processes in the stomach, esophagus, liver or vertebra. The accompanying and basic pulmonary condition is usually a secondary bronchopneumonia. Measles, bronchopneumonia and pneumothorax is a frequent example of the march of events. The perforation may be due to the rupture of a cavity, a purulent process, an emphysematous bleb or to the softening of an infarct.

Tuberculosis—While in adults at least 80 per cent. of the cases of pneumothorax are due to tuberculosis, in children not more than 40 per cent. are due to this cause.

Of this 40 per cent., the vast majority of the patients are beyond the age of four years. It has been estimated that about 1 per cent. of the cases of pulmonary tuberculosis in children develop this complication. Of the 35 cases reported by Lentz (41), 14 were due to this disease; and of the 31 cases collected by Chrzanewska (51), 12 were due to tuberculosis.

One of the earliest recorded instances of tuberculous pneumothorax in a child was reported by Leas (42). The patient was a girl, two years old, and the pneumothorax

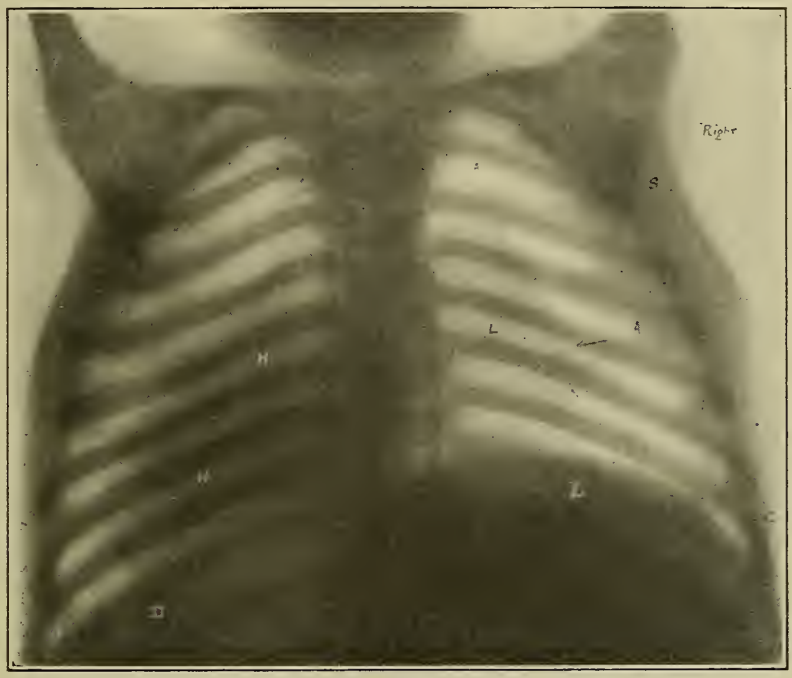

Fig. 4—Traumatic Pneumothorax.

(L) Partially collapsed lung lying at its root in the middle and posterior part of the right chest. Its three lobes can be made out. The upper extending to the fifth rib, the middle between fifth and sixth, and the lower from this point to the ninth. The arrows are one below and one above the middle lobe.
(A) Air in the right pleural cavity surrounding the lung.
(C) Costo-diaphragmatic space clear, showing no effusion.
(H) Heart displaced considerably to the left. The right and posterior border is seen at the mid-vertebral line. The portion of this right heart percussable was therefore to the right of the sternum.
(D) Diaphragm.
(S) Scapula.

was due to the rupture of a tuberculous cavity of the left lung. Sevestre reported a case in an infant of sixteen months due to rupture of a tuberculous cavity. Pollock (43) reported a case due to a similar condition in a child of three and one-half years, in whom tuberculosis had not been suspected. Parks (45), West (44), Nichols (48), Rilliet and Barthez (46), Seiffert (47), Gailliard (49), Revilliod (69), Steffen (73), Cozzolino (50) and Leconte (90) have recorded cases due to tuberculosis. The perforation usually occurs during the active stage of the disease and may be due either to the rupture of a caseous deposit or a cavity. The latter process is but rarely found in infants. The perforation is not always found within the area of the most extensive disease, and is seldom found at the apex. This is due to the protective influence of adhesions. The left side is more frequently involved, and the perforation is found more often in the lower lobe than in the upper. The perforation is, as a rule, very small and difficult of detection. Tuberculous pneumothorax usually terminates in a pyopneumothorax.

Gangrene—Gangrene of the lung is more frequently a cause of pneumothorax in children than in adults. The gangrene may be secondary to pneumonia, bronchiectasis or thrombosis. Lentz (41) mentions 11 cases due to this condition in a series of 35 cases of pneumothorax. Zuppinger (52) reported 3 cases of pneumothorax due to gangrene of an infarcted area in the course of diphtheria.

Traumatic Pneumothorax—That pneumothorax may result from trauma of the chest without any evidence of fracture was recognized as early as 1757 by Hewson (8). Traube (54) was among the first to make a contribution to this subject. It has been suggested that in these cases the injury is produced by a greenstick fracture of the rib, which rights itself when the pressure of the traumatic force is removed. This explanation probably applies only to children. It is also well known that an increase in the intrapulmonary pressure, such as may occur in compression of the chest when the glottis is closed, may result in rupture of the lung and pulmonary pleura. Many such cases have been reported in children. Hematothorax is not infrequently present in these cases. Among the cases recorded in which pneumothorax was produced by trauma without fracture or wound of chest are the following:

Curling (55): Boy, 13 years of age, was run over. Left pneumothorax resulted. No fracture or external injury could be found.

Butlin (56): Child, 6 years of age, was run over. Left pneumothorax resulted and recovery took place in six weeks. No fracture or external injury was found.

Gould (57): Child, 6 years of age, was run over. Left pneumothorax developed two days later. Chest returned to normal one week after aspiration of air. No fracture or external injury found.

Lucas (58): Boy, 2 years of age, after trauma developed right pneumothorax. Recovery took place in twenty-six days. There was no evidence of fracture.

The following case, which we were permitted to study through the courtesy of Dr. Henry M. Silver (Attending Surgeon to Beth Israel Hospital), belongs to this category:—

Hyman T., native of United States, 4½ years of age, was admitted to Beth Israel Hospital, November 27, 1907. About 4 P. M. of the day of admission he was run over by a truck. He was picked up in a fainting condition. On regaining consciousness he expectorated and vomited some blood. There was no hemorrhage from either nose or ears. There were no evidences of pain. The general condition of the child was bad. There was marked dyspnea, a feeble, thready pulse, the skin and mucous membranes were cyanotic, the peripheral circulation was poor and there was considerable shock. At 9 P. M., pulse 142, respiration 62, temperature 100.4°. Examination showed some slight discoloration of the skin over the right anterior chest, but failed to disclose any wound or any fracture of the ribs. The right chest gave all the signs of pneumothorax. The heart was considerably displaced to the left and its impulse was very feeble. Fluoroscopic examination showed the lung lying in a partially collapsed state at its root. It was motionless, except during forced expiration or coughing, when it was seen to dilate to a moderate extent. The diaphragm rose during inspiration and sank with expiration and its movement was sluggish.

For a week the condition of the child was precarious. The pulse varied from 112 to 190. The temperature was moderately elevated and fluctuated irregularly. During the second week the patient began to rally and the improvement henceforth was progressive. Ten days after the accident fluoroscopic examination showed a condition similar to that in Fig. 4. The contracted lung was seen in the middle and posterior part of the right chest, surrounded by air. During inspiration the lung could now be seen to expand from its partially shrunken state and to fill the chest cavity almost completely. With expiration, it would collapse rapidly to its root, the shrinking being of equal extent in all parts. The diaphragm on the affected side moved slightly. No fluid was visible. The patient was discharged three weeks after admission in excellent condition, with no respiratory difficulty; nevertheless, the radiograph at this time showed that there still was some air present in the affected cavity, and that the heart had not yet returned to its normal position.

Paracentesis—The production of pneumothorax during paracentesis or exploratory puncture merits consideration since it occurs more commonly than is generally supposed. Because of the absence of severe symptoms and the presence of but few physical signs, the condition is frequently overlooked. The accidental introduction of air in this way, provided no infection takes place, does not usually add to the gravity of the case, but it is not always as Stokes puts it, "a matter of trivial moment." In an appreciable number of cases it has contributed to a fatal termination. Seven deaths due to exploratory puncture of the chest are reported in the *British Journal of Children's Diseases* (53). The commonest ways in which air is thus admitted are, either through faulty technique, through injury of the lung by the point of the needle or by

leakage of air through the apparatus. The air usually enters from the exterior only after some of the fluid has been withdrawn. Fluids are incompressible, and it is therefore impossible to inject air into a chest already filled with fluid. Sears (59) reported 4 cases of pneumothorax due to paracentesis. In 3 of the cases there were no resulting bad effects, but in 1 the complication undoubtedly contributed to a fatal termination. Gittings (61) reported 3 cases with no untoward results. In one of the cases

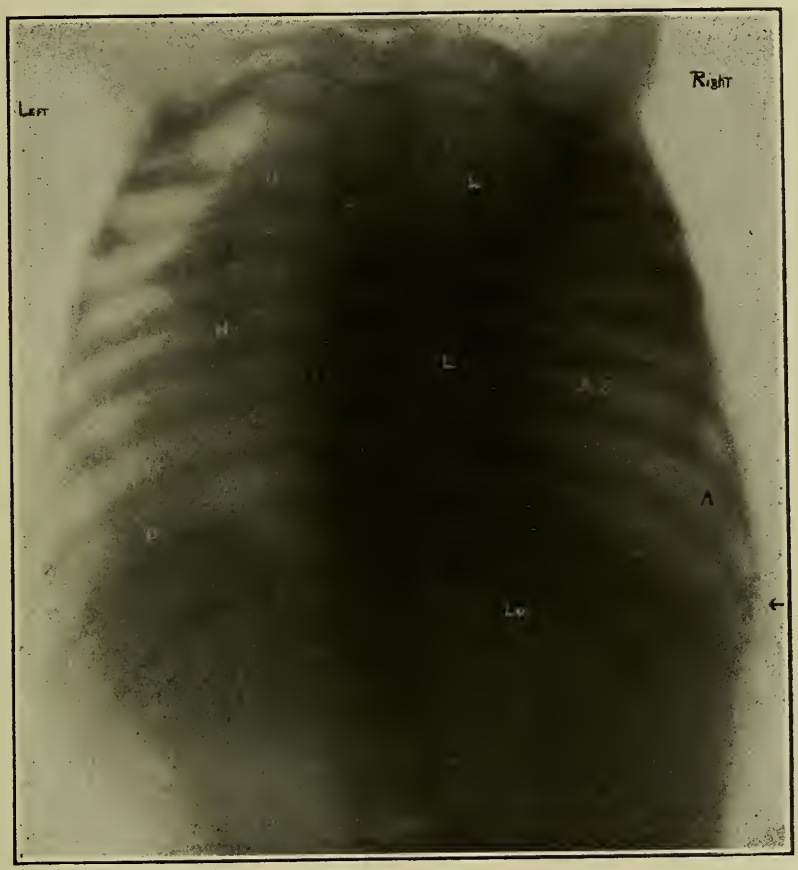

Fig. 5—Pyopneumothorax right. Ventrodorsal exposure. Recumbent posture.

(L) Collapsed lung covered by fluid.
(AE) Pleural cavity containing both air and effusion.
(A) Air bubble visible in the shadow of the antero-lateral part of the chest.
(H) Heart displaced far into left chest.
(D) Diaphragm.
(Lv) Shadow of liver merging with that of the effusion. The arrow indicates the costo-diaphragmatic space filled with fluid.

only a localized pneumothorax followed, but subcutaneous emphysema developed in all. Variot and Roy (62) reported the case of a girl of eleven years, who was tapped for pleural exudate. Immediately after tapping she developed pneumothorax. This was ascribed to rupture of the lung by pleural adhesions, but in all probability it was due directly to the trauma of paracentesis. Packard (64) reported a fatal case of pneumothorax due to perforation of an emphysematous bleb by the point of an aspirating needle. Emerson (18) reported 10 cases due to paracentesis with five deaths. Northrup (60) reported the case of a child of two years, who was admitted to the hospital suffering from severe dyspnea and cyanosis. It was operated on for empyema, but only air

escaped when the pleural cavity was opened. The pneumothorax was believed to be due to paracentesis performed before admission to the hospital.

A case of pyopneumothorax, which we believe was due to exploratory puncture, was admitted to the Children's Service of Beth Israel Hospital on September 27, 1909. The child was 5 years of age, and had had a mild attack of pertussis before the onset of the present disease. This began three weeks before admission, with fever, cough, rapid breathing and prostration. The fever was higher in the evening, and soon after the onset of the disease was associated with profuse sweats. Three days before admission the condition grew worse, the prostration became more marked, there was evidence of pain in the right chest, the temperature fluctuated between normal and 104° and the dyspnea was severe. Before admission a puncture of the chest had been made and turbid fluid withdrawn. Examination on admission showed evidence of fluid and air in the right chest. (Fig. 5.) Examination of pus obtained by puncture failed to show tubercle bacilli. The Moro and Von Pirquet tests were negative. The examination of the sputum did not show any tubercle bacilli. Ten days after admission thoracotomy was performed. Both air and pus escaped. From that time on the condition of the child gradually improved and convalescence is now progressive.*

Besides this case we have seen many others due to paracentesis and some complicated by subcutaneous emphysema. Among them was a child, three years old, seen by Dr. Huber in consultation. Exploratory puncture of the left chest had been done by the attending physician on the preceding day, because of marked dullness and feeble breathing. This procedure was followed by a pneumothorax and extensive emphysema of the back and lateral parts of the chest. A careful examination revealed, furthermore, the physical signs of an effusion on the opposite side, namely, in the right pleura. Exploratory puncture establishing the presence of pus, the right pleural cavity was incised and drained. The emphysema of the left chest wall disappeared in a few days without evidence of infection. The subsequent course, in spite of the pneumothorax on the left side, was uneventful.

Empyema—Pneumothorax produced by the perforation of a purulent effusion into the lung is not common. Such perforation occurs in the severe cases associated with gangrene of the inflammatory products and in the neglected cases. Tuberculous empyema has a tendency to follow this course. The presence of the air in the thorax may not become apparent for some time after the rupture has taken place, and even then the characteristic signs are not clearly obtained. At intervals, after severe coughing paroxysms, large quantities of foul-smelling pus may be expectorated. Comby (65) reported the case of a boy of eleven years, who developed pneumothorax three days after a purulent effusion in the left chest was noted. The perforation was found to have been produced by gangrenous degeneration of the pleura. Seifert (47) has reported a case in a boy of eight years due to rupture of a left empyema into the lung.

Foreign Bodies—Direct perforation of the lung by a foreign body aspirated into a bronchus is rare. As a rule, the perforation is caused by a secondary abscess. This complication usually occurs a long time after the foreign substance has entered the bronchus, but in exceptional cases the interval may be brief. Ast's (70) case is remarkable in this respect. The patient was a girl of four years, who had aspirated a spice into the right bronchus. Bronchopneumonia, with severe pleuritic involvement followed, and, on the eleventh day, pneumothorax. In a case reported by Zuppinger (52) of a child of two and one-half years, total right pneumothorax took place during sleep. Death followed in thirty-six hours. At autopsy the perforation was found to be due to a grain of corn which had perforated into the pleura. The foreign substance had evidently been aspirated some time before, but no history of such an occurrence had been obtained. In a case reported by Carslaw (73) the pneumothorax resulted from the perforation of the pleura by a plum stone aspirated into the right bronchus. Foreign bodies impacted in the esophagus have been known to perforate the pleura. Rosenthal (71) reported a case of pneumothorax due to the perforation of a bone impacted in the espohagus of a boy. In Müller's case, pneumothorax was produced by the perforation of the left pleura by round worms from the stomach.

Abscess—Strange as it may seem, pneumothorax due to the rupture of an abscess of the lung is a rare condition. Of Biach's 715 cases, but 10 were due to this cause. Saussier (15) cites 1 case, while Widal refers to 2. Gerard (74) cites a case of Trousseau's, and states that this form usually occurs after pneumonia in children or old people. Villey (53) believes the condition to be more common in children than in adults. Emerson (18) cites 2 cases due to metastatic abscess of the lung. In our cases the small abscess was associated with a pneumonia and empyema.

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* Since above was written, the child has been discharged cured.

Pyopneumothorax due to rupture of an abscess of the lower left lobe into an empyema. Pneumonia of the lower left lobe. Death.

B. K., 7 months old, was admitted to Beth Israel Hospital May 19, 1909, with the history of having been ill for five days with fever, cough, dyspnea and restlessness. Physical examination revealed the signs of an effusion in the left pleural cavity. On admission her pulse was 148, respiration 52, temperature 102.6°. Exploratory puncture showed turbid serum. The cytological examination of the specimen of fluid withdrawn gave 60 per cent. polynuclears and 40 per cent. mononuclears. Pneumococci were pres-

Fig. 6—Pyopneumothorax left due to paracentesis. Ventrodorsal exposure. Prone posture.

(EA) Pleural cavity containing air and effusion. Note the lighter areas of the lateral part of the chest due to the air.
(H) Heart displaced to the right.
(D) Diaphragm. On the right side it is at the level of the tenth rib, while on the left its shadow merges with that of the effusion.
(C) Costo-diaphragmatic space of normal side. Compare the appearance of this space with that on the affected side which contains fluid.
(NL) Normal lung, the seat of a compensatory emphysema.
(S) Scapula.

ent. Because of the presence of an extensive pneumonia, it was considered best to delay operation. From this time until the date of operation, the temperature ranged from 102° to 103°, on two occasions falling to 100°, and once rising to 104° F. The respiration varied between 30 and 50, and toward the end of the week rose to 64. The pulse rate fluctuated between 120 and 140, the frequency, however, gradually rising so that at the end of the week it was 170.

A white blood count, four days after admission, showed 48,000 leucocytes, of which 82 per cent. were polynuclears and 18 per cent. mononuclears. Six days after admission, on the eleventh day of the disease, vomiting and eructation appeared, which persisted to the time of death. Examination at this time showed an increase in fluid, and an exploratory puncture revealed pus. For about eight hours the condition remained unchanged, and then suddenly grew worse. Examination now showed the pres-

ence of air and fluid in the left pleural cavity. (Fig. 7.) In spite of all treatment the vomiting and eructation grew worse. Simple incision and drainage of the chest failed to give any relief. The day following the operation the blood examination showed 42,000 white blood cells, with no appreciable change in the differential count from the last examination. The temperature vacillated between 97° and 104° F., pulse varied from 120 to 170, and respiration between 34 and 60. The condition gradually grew worse, the restlessness was marked, the vomiting and eructation were persistent, muscular twitchings appeared, and eleven days after admission (sixteen days after the onset) the child died.

Only a limited autopsy was allowed. The empyema cavity was found fairly large, and apparently walled off by adhesions above on the level of the fourth dorsal spine and anteriorly about the anterior axillary line. The cavity was traversed by a few bands. The left lung showed marked consolidation of the lower lobe. About midway between the fissure and the lower border, and one inch from the posterior border, a cavity was detected, 1 cm. in diameter. The edges of the cavity were smooth; it communicated freely with the empyema cavity and was lined by pyogenic membrane 1/16 of an inch thick.

From these findings it is evident that a small abscess of the lung had set up a suppurative pleurisy, limited at first, but gradually extending, and finally, in consequence of the intractable vomiting, the adhesions had given way with the production of the pneumothorax. The exploratory puncture had been made in the usual manner, posteriorly and below the angle of the scapula, and could not in any way have caused the perforation. Previous to the autopsy, the suspicion may have existed that the pneumothorax was due to the second exploratory puncture. The post-mortem examination, however, proved this suspicion to be unfounded. The wall of the abscess cavity was not a recent one, the granulation tissue being of considerable thickness. The pleural cavity did not communicate with the lung through a narrow fistula, but directly by a wide opening. These conditions are not found in pneumothorax due to paracentesis. On the other hand, the autopsy showed that the abscess was a superficial one, associated with a pneumonic process and accompanied by a purulent effusion. The empyema was sacculated, as it very often is in infants, and the exudate contained considerable fibrin, a condition usually present in pneumococcic infections. These factors would have been sufficient under ordinary circumstances to minimize the possibility of the rupture of the abscess had not the strain of the persistent vomiting acted as an excitant.

Bovaird (40) reported the autopsy findings in 2 similar cases. In 1 case the child was four months old, and the right pleural cavity contained, in addition to the air, about 1½ ounces of thin muddy fluid. The right lung was compressed, and in its lower lobe were found two small abscess cavities about 1 cm. in diameter. One of these had perforated the pleura and produced the pneumothorax. In the other case the infant was six months old. There was left pneumothorax, and in the left upper lobe there were scattered pneumonic areas. On the anterior surface of this lobe a thin walled abscess cavity had ruptured into the pleura The lung about this abscess was consolidated and compressed.

Pertussis—Aside from the bronchopneumonia, which is a frequent and serious complication of pertussis, vesicular emphysema is present in all severe cases. As in diphtheria, these complications predispose to the production of pneumothorax, only to a greater degree. It mostly occurs, however, in debilitated children, and the process is often hastened by the combination of an inflammatory condition superimposed upon the already weakened and emphysematous lung. Thus in a case reported by Winocouroff (75) a child, four years old, after suffering from pertussis for one month, developed a croupous pneumonia, and on the third day of this disease, after a severe attack of coughing, developed pneumothorax. In Malinowski's (76) case the pneumothorax followed a paroxysm of coughing, excited by compression of the chest. In von Gelmo's (77) case the pneumothorax was accompanied by subcutaneous emphysema. In a case reported by Villy (78), a child, three years old, convalescing from diphtheria, developed pertussis and very soon after a pneumothorax.

Diphtheria—Diphtheria is a disease in which pneumothorax is not an infrequent complication or sequel. There are three complications which are rather frequent in diphtheria. The first is bronchopneumonia, which is usually of the severe type; the second is emphysema, vesicular or interstitial, and this is more common if the larynx is affected; the third is thrombosis or embolism, which may affect the vessels of the lung. These pathological conditions all predispose to the production of pneumothorax. Zuppinger (52) reports several cases in which the sequence was diphtheria, infarct, gangrene and pneumothorax. Steffen (79) reported 2 cases complicating diphtheria: one in a child of one and one-half years was due to rupture of an emphysematous lung.

and the other, in a child of five years, to softening of an infarct. Schwalbe's (80) case was a diphtheric child, who developed subcutaneous emphysema and double pneumothorax six days after a successful tracheotomy had been done. Torday (81) reported a case which followed laryngeal diphtheria. Cnopf (82) reported 4 such cases during the course of laryngeal diphtheria.

Measles—The bronchopneumonia complicating measles is usually severe and may have associated with it the pathological conditions which predispose to rupture of the

Fig. 7.—Pyopneumothorax Left. Ventrodorsal Exposure. Recumbent Posture.

(L) Collapsed and consolidated lung adherent to chest wall at point indicated by arrow.
(A) Pleural cavity containing air and effusion. The greater part of this effusion has gravitated toward the upper part of the affected chest.
(LH) Left heart. The heart is moderately displaced to the right.
(RH) Right heart.
(LD) Left diaphragm at level of eleventh rib posteriorly.
(RD) Right diaphragm at level of tenth rib posteriorly.

lung, namely, emphysema, gangrene and abscess. Zuppinger speaks of the frequency of pneumothorax during the course of severe measles. Steffen reported a case in a girl of seven years due to rupture of a small abscess. Bovaird reported 2 cases occurring during the course of measles. One was a child of four years, who, on the ninth day of measles and bronchopneumonia, went into collapse suddenly with cyanosis and dyspnea. The examination revealed a right pneumothorax. At autopsy the pleura contained about an ounce of pus, the lung was compressed and consolidated and contained bronchiectatic cavities filled with pus. The other patient was a boy of three, the pneumothorax developed on the eighteenth day of the measles. Following an exploratory puncture, subcutaneous emphysema developed, which spread over trunk and arms. At autopsy a perforation was found in the lower left lobe.

Symptoms—At the instant of the occurrence of the perforation, there is severe pain with evidence of respiratory and circulatory disturbances and shock. Elsberg (84) has proved experimentally that these symptoms are in great part due to the displacement of the mediastinal contents, which lose their support through disturbance of the equilibrium of the air pressure within the thorax. In children these symptoms are unusually severe. This is due to the mobility of their mediastinal structures. The onset is usually sudden, with severe pain, dyspnea, cyanosis and shock. As the viscera accommodate themselves to the changed conditions within the thorax the alarming symptoms subside.

It is surprising to note how quickly in many cases, particularly in older children and adults, a tolerance to the presence of air in the pleural cavity is established. Even with one lung compressed by fluid and the heart displaced, these patients are often comparatively comfortable and have but little dyspnea. This has ever been a source of wonder to clinicians. Houghton (85) in 1832 reported the case of a laborer with left pyopneumothorax, who went cheerfully about his vocation, though the succussion splash from his chest could be heard as he walked downstairs. Adams (86) reported a case in which the pneumothorax, which resulted from a slight strain, persisted without exudate or infection for a period of four years without any marked inconvenience.

Physical Examination—The child, as a rule, prefers to lie on the affected side. When the dyspnea is severe, the activity of the accessory respiratory muscles is evident. Inspection will show that one side of the chest is more or less immobile and distended. The lower ribs flare out, the intercostal spaces are widened and the depressions obliterated. The hypochondriac region corresponding to the affected side is prominent.

The cardiac impulse is displaced, and, if the left chest be affected, the heart impulse may be seen to the right of the sternum, even as far as the mammary line, and distinct epigastric pulsation will be noted.

The information gained by inspection is not characteristic of pneumothorax, since simple effusion often gives a similar picture.

Tactile fremitus is a sign not easily obtained in older children. It will, however, usually be found absent or diminished in intensity.

Percussion must be gentle, for the air in the chest makes it a sounding-board which readily exaggerates and transforms every sound and obliterates the finer differences of tone. With the exception of an area in the upper intrascapular region, the entire chest may be tympanitic from apex to base. This note will also be obtained below the level at which pulmonary resonance may be elicited normally. This is a valuable sign, and in doubtful cases will be of great service. Less frequently the note may be either hyperresonant or normal over the entire chest. There is usually an area of normal or relatively dull resonance in the intrascapular region. This is due to the more or less collapsed lung lying at its root. When the pneumothorax is due to phthisis, the apex may be adherent, and then a normal or relatively dull note will also be obtained over the upper part of the chest. Infrequently a cracked pot sound may be elicited. The absolutely flat note generally associated with effusion in the pleural cavity is seldom obtained when the effusion is associated with air; for this reason a small amount of fluid usually escapes detection, while even in the presence of a large amount it is rarely possible to accurately map out its upper level. The dull note when present will be found to shift with the position of the patient. Though this movable dullness may at times be present in simple effusion, yet in no other disease is the phenomena so marked and constant as in pneumohydrothorax.

The signs obtained by auscultation are variable and misleading. In infants the auscultatory signs differ from those in adults. The respiratory murmur is usually unchanged and succussion is seldom elicited. The metallic and amphoric qualities which the respiratory sounds possess in older children and adults are absent in infants. In older children the respiratory murmur is either entirely absent or feeble and distant. When the pneumothorax occurs in a previously healthy pleural cavity, and the lung is not diseased, the breath sounds may be harsh and loud. Whether feeble or intense, the respiratory murmur usually has an amphoric quality. This amphoric sound may be heard only over a certain part or over the entire affected chest. It is most frequently heard with expiration. In the intrascapular region the breathing may be tubular. The vocal resonance has a marked amphoric quality, and this may be present even when the respiratory murmur is absent. The so-called "metallic tinkle," which is really a râle with its pitch raised by the resonanting air chamber of the pneumothorax, may be heard at the end of expiration or during coughing. By using one coin as a plexor and one as a pleximeter, auscultation will reveal that the sound produced by the contact of the coins has been transformed into

a clear musical sound, like the note of a bell. This phenomena, first described by Trousseau, has been called the "coin sound," and was considered pathognomonic of air in the pleura. Osler (33), however, obtained this sound over a large cavity just underneath the pleura of the upper lobe. It cannot be denied that it is a sign of great value in children, in whom large cavitation of the lung is a rare condition. Over the fluid no respiratory sounds are obtained. By shaking the child, either in the recumbent or erect posture, the ancient sign "Succussio Hippocratis," a splashing sound may be heard if the amount of air associated with the fluid is not too small.

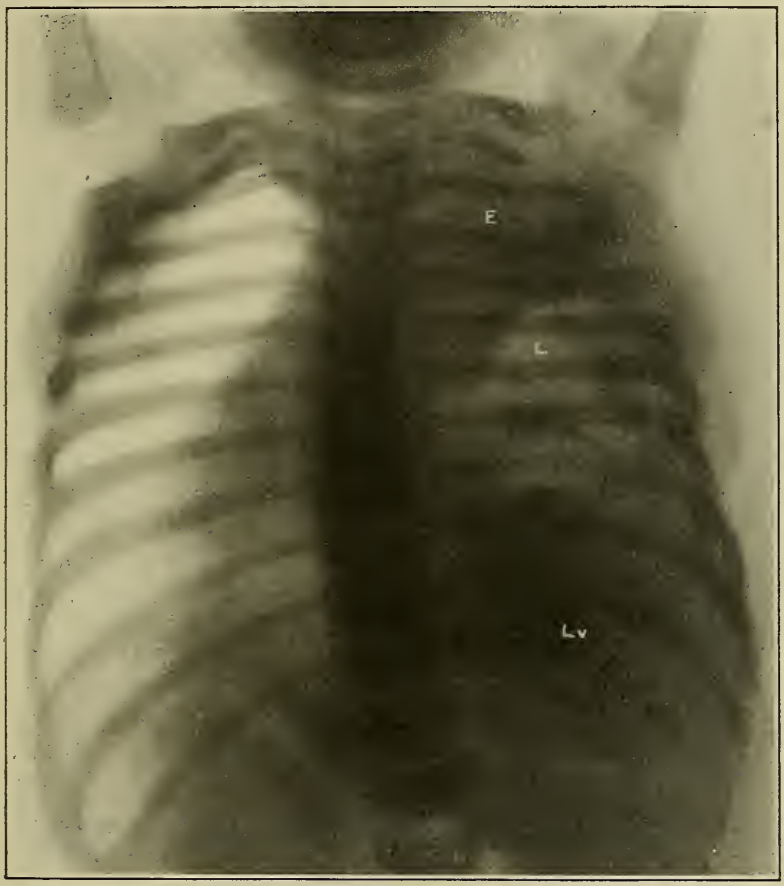

Fig. 8—Right pyopneumothorax. Ventrodorsal exposure. Recumbent posture.

(E) Effusion.
(L) Partially collapsed lung adherent to posterior chest wall and unable to retract completely.
(H) Heart displaced to the left.
(Lv) Shadow of the liver merging with that of the effusion. Compare the costo-diaphragmatic spaces. Note the presence of fluid in that of the right side.

Examination with the Roentgen Ray—The value of the Roentgen ray examination, in the study of the varied conditions present in pneumothorax, cannot be overestimated. It gives such accurate information concerning certain of the pathological conditions as is not obtainable in any other way. It makes possible the visual examination of the movements of the affected viscera and permits the systematic study of the progress of the disease. Valuable as this examination is, however, in furnishing important data, it should not be considered as a procedure which is to replace the older established methods of diagnosis, but rather is it to be held as a supplementary

diagnostic method of undoubted accuracy. The difficulties which present themselves in the diagnosis of pneumothorax demand that all the diagnostic means at our disposal be employed in the effort to obtain a true idea of the conditions existing in this disease.

The examination may be made either with the aid of the fluorescent screen (Roentgenoscopy), which permits the study of the movements of the thoracic viscera, or a record of the pathological conditions may be obtained upon the photographic plate (Roentgenography). Both methods are to be employed, and the examination cannot be considered complete without either. For no description, however, accurate, of the fleeting image seen upon the fluorescent screen can compare as a graphic record with the permanent impression on a photographic plate, which also gives the finer structural detail not to be seen with the screen. The picture of pneumothorax is so striking and characteristic that once seen the condition is thereafter easily recognized.

For the clear understanding of the conditions within the affected chest, information is necessary regarding the following points, upon which the Roentgen ray examination gives the required data:—

First—Degree of Pneumothorax—Has the air invaded the entire cavity or is it confined by adhesions to a particular part of the chest? The shadow of the normal lung as compared to that cast by the spine and mediastinal structures is bright, because the ray penetrates the air-containing tissues with greater ease than it does the dense structure. So also the shadow grows brighter during inspiration. With respiration, the movement of the normal lung shadows are visible. When air is present in the pleural cavity, however, the whole one part of the chest will be brilliantly illuminated. The ray will so affect the screen or plate as if nothing had been interposed in its course. The contrast between the part thus illuminated and the central dense structures is now very marked. Closer examination of this brilliant area will show that the normal lung markings are absent, while midway in the chest and against the spinal column an irregularly oval shadow with a well-defined outline will be noted. This shadow may enlarge and grow lighter during one or the other phases of respiration. The brilliantly illuminated part of the chest is that in which the pleural cavity contains air, while the mobile shadow against the spinal column is the more or less collapsed lung. Because of this collapse the penetration of the ray is facilitated, thus accounting for the brightness of the affected chest. The lattice-work effect of the ribs over the bright area is very clear, very distinct and of a lighter shade than the ribs on the normal side, while the structural detail of the ribs over this bright area are more clearly visible than on the normal side. The costo-diaphragmatic space is sharply defined and should always be examined for the presence of effusion. When, as in Figures 1, 4, 10 and 11, the air occupies every part of the pleural cavity, this characteristic appearance is present over the entire side, while, if the air is localized, only a circumscribed part of the chest will give the picture. The only other appearance which may simulate that of a localized pneumothorax is a cavity in the lung. In the latter condition, however, the contrast between the normal and abnormal tissue is not so marked and the lighter area indicating the lung cavity is surrounded by a distinct ring of dense shadow corresponding to the cavity wall. Examination by the oblique method will also be of value in this differentiation.

Second—Condition of the Lung—Is the lung normal or diseased? Is it completely or only partially collapsed? Tuberculosis, pneumonia and abscess are all demonstrable. When the lung is completely collapsed it may be impossible to definitely demonstrate the diffuse infiltration of a tuberculosis, but in such a case evidences of this disease will usually be found in the other lung. A large area of consolidation will not permit the lung to collapse to a marked extent. Occasionally the clue to the pathological primary process is derived from the condition of a part of the lung adherent. and therefore unable to retract. The lobes of the collapsed lung may be differentiated (Fig. 4), and in some cases one or other of the lobes not only contains more air, but distends to a greater extent during respiration. It is perhaps not an unjustified assumption that the more collapsed and more immobile lobe bears the perforation.

Third—Position and Mobility of the Lung—What is the position of the retracted lung? Does it functionate? If free to collapse, the lung is always found lying at its root. For some time after the perforation has occurred, the collapse is not complete. The lung still contains considerable air and casts a distinct shadow of considerable extent with a sharply defined border. When the causes which make for restitution are not at play, then the air in the collapsed lung is gradually absorbed; and as this progresses, the lung continues to shrink, so that in old cases it is to be seen lying airless and motionless, a ribbon-like mass, along the spinal column, as in Figure 10.

In closed pneumothorax, when the lung takes an active part in respiration, its appearance is as shown in Figures 4, 9 and 11. In these cases the lung may be ob-

served during respiratory movements to expand from its shrunken state, distend so as to almost completely fill the chest, and then retract to its former partially collapsed condition at its root. Under certain conditions this movement of the partially collapsed lung is what is termed paradoxical; that is to say, instead of dilating with inspiration, the lung is inflated during expiration, and it is this expiratory force derived

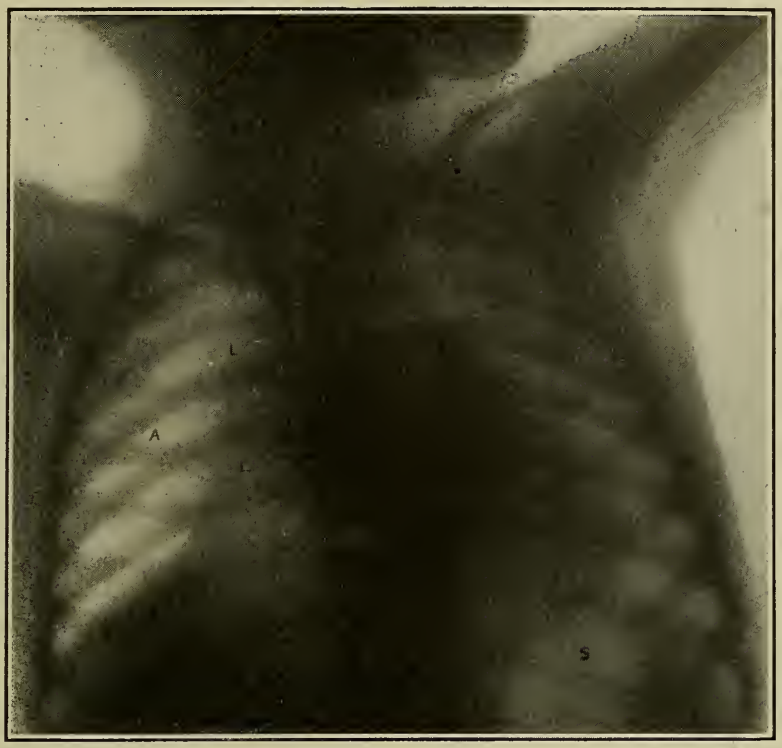

Fig. 9—Pneumothorax right. Dorsaventral view. (Plate to sternum.)

(L) Collapsed lung.
(A) Air in pleural cavity.
(D) Diaphragm.
(H) Heart displaced considerably to the left.
(S) Stomach—distended by gas.

from the intact emphysematous (compensatory) lung which is the important factor in the restitution of conditions to the normal.

Fourth—Condition of the Pleura—Does it contain effusion? The difficulty of detecting by the usual diagnostic means, either the presence or the amount of effusion within a pleural cavity containing air, is well known to every clinician. With the aid of the Roentgen ray the smallest effusion may be detected. The costodiaphragmatic space should first be examined, and if this is clear there is no free effusion. The picture of the chest in hydropneumothorax will show three zones of shadow which differ in the intensity of their illumination. (Fig. 2.) There is a bright upper zone, a brilliant middle zone, and a dark lower zone. The bright upper zone corresponds to a part of the collapsed lung retracted and pressed against the upper and posterior part of the chest. The middle brilliant zone represents the part of the chest containing air. The contrast between this zone and the dark zone beneath it is very marked. This lower zone represents the fluid. It is a dense homogeneous shadow which may obscure the shadow of the ribs. Below it merges without any defined boundary into the shadow of the liver, while its upper level is sharply defined and perfectly horizontal. This upper level is sharply defined no matter how small the quantity of air. In simple effusion, on the other hand, there is no sharp line of demarcation at the

level of the fluid, but the shadow of the latter gradually merges into that of the compressed lung. This level of the fluid in hydropneumothorax remains horizontal whatever the position of the thorax. When the effusion occurs late, that is, after the collapsed lung has become airless, or if the condition is an old one, then but two zones will be seen an upper brilliant zone corresponding to the air and a lower dark zone

Fig. 10—Pneumothorax. To show the collapsed lung (L) lying as a ribbon-like mass along the spinal column. Note the distinctness of the ribs of that part of the pleural cavity (A) containing but air. (CS) Indicates the costo-diaphragmatic sinus.

Fig. 11—Pneumothorax. To show a collapsed lung which still contains considerable air and which was observed to distend and shrink with respiratory movements.

corresponding to the fluid. The lung in these cases lies against the spinal column and its shadow merges with that of the mediastinum. This is the picture when the patient is examined in the upright position. With children, however, it is usually neither feasible nor advisable to examine them in the erect posture, and almost impossible to Roentgenograph them in this position. But when lying down, in which position they are best examined, the fluid flows over the posterior wall of the chest, while the air rises above it. The picture now obtained is a little more difficult of

interpretation. (Fig. 3 and Fig. 5). Instead of two sharply contrasted zones indicating the air and fluid, the entire chest is obscured by a light shadow, and it is only at the sides that the brilliant illumination due to the air is visible. The lung, however, still holds its position at the root. The motion of the fluid in response to the movements of the chest, diaphragm and heart has already been discussed. The parodoxical movement of the fluid may be studied. So passive is the diaphragm in some of these cases that sudden pressure upon the abdomen will cause a rise of the level of the fluid.

Fifth—Position and Movement of Diaphragm—What is the position of this muscle, and how and to what degree is its motion affected and limited? Once retraction of the lung occurs, the movements of the diaphragm are inhibited, and its dome becomes flattened. When the lung is collapsed to a marked degree this muscle appears to lose its tone and passively rises and falls in response to the movement of the abdominal viscera. Its movement under these conditions is the reverse of its normal action.

Sixth—The position of the Heart—Are the mediastinal contents displaced, and to what extent? The position of the heart may serve as an index to the amount of air in the pleural cavity, for the greater the quantity of air the greater the displacement. The displacement is more marked when the left pleural cavity is involved, and when there is effusion in addition to the air. In disease of the left pleura, the entire heart may be pushed into the right chest. Under these circumstances there is also a rotation of the organ, so that the left ventricle lies more anteriorly. A dilatation of the pulmonary artery and left auricle may be noted.

Seventh—The Condition of the Chest Wall—Are fractures present? A fracture must be looked for in all cases due to trauma. The patient should be examined in all positions, and in children the parts of the ribs at the epiphyseal junction should be carefully examined.

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ADULT SYPHILIS OF THE LUNG: WITH A CASE REPORT.*

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It seems quite probable that syphilitic lesions of the lung in adults occur much more frequently than they are diagnosticated, the chief reason why such processes are not demonstrated during life being the resemblance of their physical signs to those of certain types of pulmonary tuberculosis.

Bériel (1) states that acquired lues of the adult lung is common, but the specific nature of the affection must be deduced from its occurrence with syphilitic lesions elsewhere in the body. He considers that two types may be described. 1.—Catarrhal pneumonia or the desquamative bronchopneumonia of Homolle. This is characterized by the presence in the alveolus of a considerable amount of large cellular elements, more or less changed. The liquid exudate, which is at times present, gives to these lesions, on macroscopic examination, a peculiar appearance which Hiller has termed gelatinous pneumonia. 2.—The so-called interstitial pneumonia, of which the principal

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feature is the increase in thickness of the interstitial framework of the lung with infiltration of its whole tissue Of these two types the second, with its varieties, seems to be more directly due to syphilitic infection, and it represents the true syphilitic pneumonia.

Such pneumonic processes as the above may result in a cicatricial sclerosis which may occur in bands, *en bloc,* or at the nucleus of gummata (these, according to Virchow, result from connective tissue proliferation) simulating at first, in their growth, granulation tissue. The later development of gummatous tumors may take place in

Figure 1.—Showing the dilated veins in the chest and abdomen.

one of two ways. Either the cellular formation prevails, the intercellular substance rapidly softening and becoming gelatinous, mucoid or fluid, and the tumor degenerates, becomes puriform, opens outward, and ulcerates, or, on the other hand, the cellular elements being not very abundant, the intercellular substance increases, the cells preserving the fusiform or star-shaped character of connective tissue cells or assuming the round shape of those of granulation tissue. Later the cells become fatty and the dry, yellow node of visceral syphilis is formed.

Keyes (2) describes the lesions of pulmonary lues in adults as being either soft or hard, according to their density; this density depending upon the age of the process and upon the transformation of the exudate into organized tissue. This sclerosis

is the usual lesion of acquired syphilis of the lung. It is likely to be of irregular distribution and is more common in the lower than in the upper lobes and in the right than in the left lung. The sclerotic tissue is hard, grayish white, or blackish, and very retractile; it may occur in bands radiating from a central point or in nodular masses which are often beneath the pleura; fibrous peribronchitis may be present. With the luetic interstitial changes there are usually bronchiectatic cavities of various shapes and sizes. Often such a cavity is the chief lesion and may be of considerable size; it may contain pus or its walls may be necrotic and gangrenous, like those of tuberculous cavities. Keyes also states that, while mixed infection with the bacillus tuberculosis is said to be common, it is likely that many of the classical instances of pulmonary syphilis are merely irregular tuberculous processes and that the frequency of the coexistence of the two affections has been overestimated although a few authentic cases have been recorded. He quotes Tripier and Bériel as holding that most instances of bronchiectasis are due to unsuspected syphilis of the lung.

With regard to the existence of simple connective tissue hypertrophy of the pulmonary framework Virchow maintains (3) that there may occur simple irritative affections of the lungs of luetic origin which never become gummatous, and he is inclined to regard certain fibrous forms of pleuritis, of pneumonia, and of peribronchitis as analogous to the chronic syphilitic inflammations of the liver and other viscera.

Rollet (3) has demonstrated that pulmonary syphiloma may appear not only in nodular masses of irregular size and differing shape, but also as a diffuse infiltration, which, alone or in connection with nodules, may extend over a pulmonary lobe.

Schnitzler (3) describes diffuse syphilitic disease of the lungs in which the organ is generally of firmer consistency, of greater weight, and of more uniform surface. The infiltration extends over one or both lungs or over only a part of them. The infiltrated parts are, as a rule, entirely airless, grayish red or grayish yellow, smooth, homogeneous, with a scanty turbid juice. The bronchi are usually of normal caliber are filled with much purulent mucus and little air. The pathology of this type of pulmonary syphilis seems to coincide with the condition in the case reported subsequently as evidenced by the physical signs and radiographic picture.

With regard to the presence of the *Spirocheta pallida* in the lesions of acquired syphilis of the lung Levaditi and Roche state that, in contradistinction to the lesions of hereditary syphilis, the spirocheta is rarely found in the lesions of acquired lues. It has been found, in specific aortitis, in the wall of the aorta, in the suprarenal capsules, and possibly in hepatic gummata.

Concerning the association of syphilis and tuberculosis of the lung Maurice [see Bériel (1)] considers that in the lungs, as elsewhere, the two affections remain independent and do not affect one another in any marked degree despite the analogy and strong resemblance of their lesions. Neither do they combine to form hybrid products endowed with power to transmit themselves. Their combined presence is merely juxtaposition and does not create mixed forms of tuberculosyphilitic pneumopathy. Their association occurs in various types: 1.—With manifest and extensive syphilitic lesions there may be histologic changes referable to tuberculosis, but the lesions and symptoms are not modified by the association. 2.—Inversely, in tuberculous patients who are also syphilitic there may be, in the neighborhood of the bacillary lesions, histologic features of luetic nature. 3.—In apposition to the preceding types, which are frequent, is the type in which marked tuberculous and syphilitic lesions coexist. Here the clinical aspect is such that the diagnosis is almost impossible: the luetic affection is not recognized and the tuberculous process alone is diagnosticated.

Fournier (5) views the association of tuberculosis and syphilis from three clinical aspects: 1.—When syphilis is engrafted upon a proved case of tuberculosis the course of the latter becomes more rapid and severe. 2.—When the tuberculous infection appears during the early stages of lues. Here also the prognosis is grave and the course of the tuberculous infection is almost always rapid (Jacquinet). 3.—When tuberculosis is engrafted upon an old syphilitic process (Landouzy) the disease assumes a form of fibrosis of tardy, sluggish, afebrile evolution. The bacillus appears to live as a parasite upon the surface of the syphilitic cavities in the lung without causing ulceration. The patient may survive for a considerable period and may appear to be doing well.

With regard to the differentiation of tuberculosis and syphilis of the lung the same author gives the following points: 1.—Absence of tubercle bacilli in the sputum is a negative point of great importance. Repeated examination is an essential as also are continued negative results. Syphilis is probable in the persistent absence of bacilli, cancer cells, or evidence of hydatid disease. 2.—Character of the local lesion. Syphilis is unilateral, circumscribed, and has no predilection for the apices of the lungs. It

must be remembered, in this connection, that tuberculosis also may begin in one lung only and that it is possible for lues to affect both lungs simultaneously. Pulmonary syphilis is usually circumscribed while tuberculosis is more likely to be disseminated. Tuberculosis usually begins at an apex. Syphilis is less discriminating; it may occur in the lower, middle, or upper lobe. Its preference is for the middle of the organ in the neighborhood of the hilum. 3.—General symptoms: tuberculosis affects the constitutional condition and causes the well-known train of symptoms; emaciation,

Figure 2.—Skiagram of the thorax of T. B.

weakness, anorexia, dyspepsia, diarrhea, rise of temperature, etc. Syphilis does not influence the appetite or the nutrition, as a rule; if the general health is impaired such impairment is of slow and gradual evolution. 4.—The course of tuberculosis is likely to be rapid while that of syphilis is tardy.

According to Bériel, for the diagnosis of pulmonary syphilis are necessary: 1.—Assurance of a previous leutic infection. 2.—Presence of other visceral lesions of evident specific character. 3.—The certainty that the lesions are not due to infection of other type—especially tuberculosis.

To discuss these three considerations in order: the history, if negative, is of little importance. Syphilitic subjects may present lesions of diverse nature and characteristic manifestations may be absent in patients plainly luetic. A denial of specific disease should never be considered to exclude pulmonary syphilis.

The presence of other specific lesions in various viscera, such as hepatic gummata, laryngeal changes (which are frequent in pulmonary syphilis) aids in the diagnosis. The existence of parasyphilitic alterations, such as spinal tabes, specific aortitis, aneurism, etc., is also of assistance. Still these lesions and signs of infection may be absent in true lues of the lungs and present in tuberculosis.

Laboratory and other clinical tests made with a view to the elimination of tuberculosis are also insufficient criteria by themselves and likewise have the great disadvantage that, like all negative proofs, they are inconclusive. Absence of bacilli in

exudates or sections is no proof of syphilis; negative inoculations do not rule out tuberculosis, and even in positive reports the hypothesis of specific disease cannot be excluded. The presence of the tubercle bacillus is a criterion in favor of tuberculosis but it does not exclude the possible coexistence of syphilis. Successful inoculations also afford an unsatisfactory affirmation for the same reason. Such tests are useful only in that they, when positive, prove the presence of tuberculosis. As stated previously the *Spirocheta pallida* is most unlikely to be found in the lesions of adult syphilis of the lung and the presence or absence of the Wassermann reaction is as unconfirmatory as are the laboratory and other tests for tuberculosis.

Case Report—T. B., an intelligent man, 46 years of age, a cook by trade, came under the writer's notice in September, 1908. He was first seen at the tuberculosis dispensary of Bellevue Hospital and was immediately admitted to the ward.

Family History—Negative as regards syphilis and tuberculosis.

Previous History—Measles and whooping cough in childhood; chancre fourteen years ago, followed by the usual secondaries on skin and mucous membranes; irregular treatment for two years. Gonorrhoea nine years ago. Served in the Spanish war and had malaria and (probably) typhoid fever during his service. About seven years ago he noticed a swollen vein on the right side of the neck and a feeling of dizziness on stooping. This swelling disappeared and a dilatation of the veins showed itself just inside the front of the right shoulder; soon the veins of the right arm became swollen down as far as the elbow and the superficial veins of the chest and abdomen began to enlarge on the right side. Three years ago the veins of the left arm and of the left side of the chest and abdomen also became swollen and prominent. About one year ago he suffered from what was apparently an attack of acute nephritis but recovered. He had been accustomed to indulge in alcohol to a considerable degree.

Present History—About four years ago the patient began to lose flesh and strength and developed a cough which has persisted ever since. Three months later he expectorated some blood. Blood has appeared in his sputum (which has been profuse and mucopurulent) from time to time ever since. There has been up to this time no sudden expectoration of a considerable amount of matter followed by a diminution of the cough and expectoration. He has had no night sweats, feverish, or chilly feelings. He has been treated at intervals for tuberculosis of the lungs, but says that his physicians have never been sure of the diagnosis. In November, 1907, he entered a sanatorium in Texas where he remained for six months. While there he received numerous hypodermatic injections of tuberculin for the purpose of diagnosis, but says there was never any positive reaction. His sputum has been examined many times but tubercle bacilli have never been found. While at the sanatorium he improved, but began to suffer from pain in the left upper jaw in the region of the canine tooth. This pain later spread so as to affect the entire left side of his face and head and is still present. The pain is severe, deep, and boring in character with occasional sharp, shooting pains in the left eye and ear. About a month ago he noticed that he could not move the left eye outward. He complains chiefly of cough, with thick, yellowish, mucopurulent sputum which is sometimes bloody, general weakness, pain in the left side of head, and poor eyesight.

Physical Examination—The patient is poorly nourished (weight 114 lbs.), his face is red and congested and is somewhat more full on the left side. There is slight left exophthalmos and paralysis of the external rectus of the left eye. The pupils are normal; there is marked clubbing of the fingers. The superficial veins of the arms are dilated. The radial arteries are moderately thickened. The thorax is symmetrical, elongated and barrel-shaped; the costal margins are everted. The superficial veins are enlarged, tortuous, and distended, more especially on the right side. (See Fig. 1.) Heart: The apex impulse is not definitely localized; the cardiac dullness is obscured; the apex beat is heard loudest over the sternum just above the ensiform cartilage. The heart action is regular, there are no murmurs; the aortic second sound is accentuated. Lungs: There is diminished expansion of the right lung; the vocal fremitus over the entire right lung is increased except at the base behind, where it is normal. The note upon precussion is dull in front as far as the third rib, it is flat below this point; behind, the note is dull to the midscapular region and flat below this point. The breathing over back and front is broncho-vesicular; the voice is bronchial, especially so over the lower lobe. On admission there were numerous fine râles over both back and front; later these disappeared. The left lung gives the usual signs of compensatory emphysema with the addition of slight dullness at the apex and a few fine râles here and at the base behind. An X-ray photograph of the thorax was taken (see Fig. 2). The abdomen is scaphoid in shape; the superficial veins are dilated and tortuous. The liver is palpable about one inch below the costal margin. The reflexes are normal. Laryn-

goscopic examination reveals no abnormality. Ophthalmoscopic examination shows the presence of a choroiditis and retinitis of evident syphilitic nature. (See Fig. 3.)

The patient's sputum was carefully examined for the presence of the tubercle bacillus, always with a negative result. Inoculation tests were also made, the inoculated guinea-pig remaining alive and healthy after six weeks had elapsed. The ophthalmic test (0.025 cc. of ½ per cent. tuberculin) was employed and gave a doubtful positive reaction. This measure was taken before the choroiditis had been demonstrated, otherwise it probably would not have been used. It caused only a slight reddening of the conjunctiva. The cutaneous reaction (50 per cent. tuberculin) produced a moderately positive result. Injections of 1.5 mg. and 4.5 mg. of tuberculin caused no diagnostic reaction, but following an injection of 9 mg. the patient's temperature rose to 101.5 deg. Fahr.; there were, however, no marked constitutional symptoms. Exploration of the pleural cavity did not reveal the presence of fluid.

The Wassermann reaction was not employed because it seemed unnecessary. Had it been positive nothing would have been proven concerning the pulmonary condition,

Figure 3.—Fundus of the eye of T. B., showing disseminated syphilitic choroiditis.

and had it been negative one would have hesitated to rule out syphilis on account of the history, the characteristic ophthalmic lesion, and the prompt improvement of the patient when put upon antiluetic treatment.

During the twenty-six days that the patient remained in the hospital his temperature was never above 99.5° F., except following the injection of tuberculin mentioned previously, and for the most part it was slightly below normal. The weight rapidly increased to 132 lbs. and the patient gained markedly in strength. Under massive doses of potassium iodide and small doses of mercury bichloride the pain in the face disappeared and the visual disorder became greatly ameliorated.

The patient was discharged at his own request since he wished to resume work. He was seen a few days later at the Presbyterian Hospital Out-Patient Department, where the accompanying X-ray photograph was taken; at this time he felt in good condition, complaining only of cough with occasional bloody expectoration. The physical signs were practically as when first seen except that the râles at the apex of the left lung had disappeared. He was advised to continue taking potassium iodide. Since this time he has not been heard from, his work having taken him out of the city.

I have recently learned that the patient spent several weeks at the New York Health Department's Sanatorium for Tuberculosis at Otisville, N. Y., in the summer of 1909. During this time his sputum was examined three times for tubercle bacilli with negative results, and Dr. E. S. McSweeny, the physician in charge of the institution, has informed me that he considered the case an instance of pulmonary syphilis.

It would seem to the writer that this is, very probably, an instance of acquired syphilis of the lung; whether there has, rather recently, been engrafted upon the luetic

process an infection with tuberculosis is debatable. The positive reaction to the tuberculin injection appears to point toward that possibility. At any rate a consideration of the case, if it will show nothing else, will demonstrate the difficulties with which the diagnosis of pulmonary lues *intra vitam* is fraught.

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THE DIAGNOSIS AND TREATMENT OF PEPTIC ULCER.*

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During the last twenty years a vast literature has accumulated regarding the subject of stomach disorders. Specialists in gastroenterology have elaborated the importance of this or that clinical symptom of stomach indigestion, with a refinement of nomenclature and with an emphasis of utterance more remarkable for its fervor than for its importance to the sick man. A part has been magnified at the expense of the whole, and, in our desire as general practitioners to understand the intricacies of specialism, we have been led into the error of treating a sick stomach instead of trying to cure a sick man. Faddists in diet have been hailed as prophets, and ingenious mechanical and electrical local devices have been sought for, to improve men going down under the stress and strain of modern life, instead of securing for these men restful sleep, fresh air, sunlight, physical exercise, proper activity of the bowels, kidneys, and skin, and that mental content which comes with a realization of the fact that the chief end of life is not the accumulation of riches and honors.

The individual equation in disease has given place to the "feudality of classification and the tyranny of established rule" (1). We have been led away from the fact that while each factor of the digestive process has its own function to perform, all are interrelated, not only with all other factors of the alimentary apparatus, but also with all the other mechanisms of our organism, and especially with our nervous functions and with our mental processes. But while this absolute interrelational integrity must, as a rule, be maintained for the purpose of perfect health, nutrition may be kept up in exceptional cases, even after the removal of the entire stomach by surgical intervention, or in the almost complete absence of hydrochloric acid from the stomach, seen in certain cases of progressive pernicious anemia. Nature here, as elsewhere, seems capable of applying the principles of adaptability and vicarious action. We must also bear in mind that the accurate, complete, and painstaking researches of that pioneer American physiologist, Beaumont, demonstrated, as long ago as 1823, that the recuperative and regenerative power of the stomach was sufficient to atone not only for violent inflammation, but for extensive trauma.

Before we can apply these principles to the consideration of the subject of peptic ulcer, it is necessary to define exactly what is meant by that term. The gastric mucosa, like other surfaces of the body, may suffer ulceration from chemical, mechanical, or toxic irritants, the acute infections, tuberculosis, syphilis, scurvy, diabetes, and puerperal septicemia, but it is scarcely proper to regard these as cases of peptic ulcer, even though they may be produced by the eroding action of the gastric juice upon devitalized tissue. True peptic ulcer is none of these, but is "a more or less progressive destruction beginning in the mucosa and sometimes extending to and even through the deeper layers of the stomach wall, of the nature of a degeneration or a necrosis" (2). Sometimes we recognize this condition easily at the bedside, but at other times it is found only in the deadhouse in cases unrecognized during life. In one thousand

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consecutive autopsies at Bellevue Hospital, Harlow Brooks found it existing in nine bodies, in only two of which had it been discovered before death (3). Cases fall into two groups: 1.—Acute peptic ulcer in chlorotic young women; 2.—Chronic or indurated peptic ulcer in men past middle life. Apparently then there is some common factor which lowers vitality of tissue and is operative in early adult life of women and after middle life in men. This factor is at present unknown, but there is much analogy to suggest that it may be a trophoneurosis akin in its manifestations to the visceral lesions, apparently secondary to neurotrophic disturbance, which sometimes occur in angioneurotic edema (1). This trophoneurosis may be the factor which, added to destruction of gastric epithelium with disturbance of the circulation in the stomach and hyperacidity of the gastric juice, produces the combination permitting autodigestion. Erosion alone does not cause peptic ulcer, blood stasis in the gastric circulation exists only in a few isolated cases and is not found in the thousands of cardiac cases where we would naturally expect it to occur, and hyperchlorhydria exists in thousands of other cases without producing peptic ulcer when the nervous system is not below par by reason of overwork, underfeeding, business troubles, or domestic infelicities (4). Again, hyperacidity is by no means constant in gastric ulcer, although when it does exist it may prevent healing of the ulcer and may cause it to become chronic.

Absence of this neurotrophic disturbance then may be the answer to that question which has always puzzled us, "Why does not the normal healthy stomach digest itself?" Another answer is, however, clamoring for recognition in the literature. This is based on the idea that certain endogenic and exogenic poisons, which select the gastric mucous membrane for their special region of attack, contribute to the formation of typical round ulcer of the stomach (5). And Weinland has described an antipepsin ferment which was supposed to reside in and to form part of the gland cells, thus intimately protecting the same from autodigestion by these poisons, and has stated that local deficiency of these antibodies was the predominant factor. But how are we to explain this local deficiency? Turck has produced genuine induced round ulcers in every experiment in which he fed bouillon cultures of the colon bacillus to dogs and believes that the etiology is dual: 1.—There is some toxic status which overcomes the natural resistance, resulting in cytolysis; 2.—Some chemical substances are formed in the alimentary tract, which, when absorbed, neutralize the protective bodies in the blood and tissues, resulting in autocytolysis.

The cardinal symptoms of gastric ulcer are pain after eating, epigastric tenderness, vomiting usually of very acid material, hematemesis, and blood in the stools. Blood in the vomitus and feces may not be obvious, and microsopic, spectroscopic, microchemical and chemical tests for its determination may be required. Secondary symptoms are anemia, emaciation, weakness, nervousness, melancholia, headache, thirst and constipation. Complications due to hemorrhage, perforation, fistula, subphrenic abscess, perigastritis with adhesions, distortions of the stomach due to indurative and contractive changes around the ulcer, and carcinoma developing on the site of a chronic ulcer, will each add its own modification of the typical picture.

The objective signs elicited by physical examination add but little information to the patient's story. Localized tenderness is the most valuable sign. Palpable tumor may sometimes be felt in chronic ulcer, either from the thickened ulcer itself, from muscular hypertrophy or adhesions, or from exudate. The results from gastric analysis are very variable, according to the type of the ulcer. The finding of blood in the gastric contents or in the stools is of more importance than any other sign.

When this typical combination of symptoms and sign exists, there is very little doubt as to diagnosis, but in many cases both symptoms and signs are very indefinite and diagnosis is obscure. In the differential diagnosis we must exclude gastralgia, hyperesthesia, hyperchlorhydria, hysteria, gastritis, pregnancy with hyperemesis, uremia, cancer, gallstones and renal stones, aneurysm of the abdominal aorta, gastric crisis in spinal diseases, and hemorrhagic erosions with exfoliation. In gastralgia the pain bears no relation to taking of food, pressure relieves the pain, blood is absent. Yet more than one case treated as gastralgia for a long time has confounded the medical attendant by eventuating in a copious hematemesis. Simple hyperchlorhydria rarely has vomiting or hematemesis, very little tenderness, pain appears long after food or at night, proper albuminous diet with alkalies usually promptly relieves. Simple hyperesthesia shows pain at once after meals, irrespective of kind of food or of its temperature. Hysteria has no severe pain as a rule, but prompt vomiting after eating, and shows the stigmata of hysteria elsewhere. Gastritis has obvious dietetic indiscretion, usually fever, anorexia, toxemia and tenderness and pain which are diffused. Uremia shows characteristic urinary findings. Cancer will often have debility and emaciation preceding the other signs; the pain is more constant and more independent of food; vomiting gives less relief than in ulcer, the vomitus shows little

or no hydrochloric acid, and may show lactic acid after a Boas test meal together with ill-digested food and the Boas-Oppler bacilli; if hematemesis occurs, it will be of coffee-ground type. In chronic ulcer causing a pyloric tumor with dilatation of the stomach the differentiation may be impossible—before operation. When cancer is engrafted upon an old ulcer, there is increase in pain, gradual lessening of hydrochloric acid, and tumor increasing in size and assuming a more nodular character. The crucial test for hemorrhagic erosions with exfoliation is the finding in the lavage water of bits of mucous membrane, but these have been found in many stomach conditions without hemorrhage.

Gallstones may present every symptom of gastric or duodenal ulcer, and experienced surgeons have often been deceived. The importance of testing of urine for biliverdin by Rosin's test in every suspected case has lately been brought forward (7). Spinal disease usually has symptoms and signs which can be elicited by physicians who take the trouble to make routine neurological examinations of their cases.

Duodenal ulcer was formerly described independently of gastric ulcer and was thought to exist in about 6.6 per cent. of all peptic ulcers only, but the surgery of recent years has shown that the proportion is ever increasing and is perhaps 1 to 1. In the last reported 200 cases of the Mayos, 98 were duodenal, 87 were gastric, and 15 were independent of each viscus (2). Duodenal ulcer depends upon the same main etiological factors as gastric ulcer, and its symptomatology is almost identical. Cases present under four types: 1.—Those indistinguishable from gastric ulcer in symptoms and signs; 2.—Those with hemorrhages from the stomach or bowel, or both, and with no other symptoms; 3.—Those with symptoms resembling biliary colic, especially the pain, tenderness and intermittent jaundice; 4.—The perforative cases which simulate also gallbladder perforations and appendicitis. Einhorn believes that he can make the diagnosis clinically with some certainty by the thread test showing a distinct blood spot at a distance of 58 to 60 cm. from the teeth (8).

In the treatment of gastric ulcer prophylaxis is difficult because the etiology is obscure. Curative treatment must first take cognizance of the variety of ulcer present, whether acute or chronic. Study in the post-mortem room shows that four out of five cases of simple acute gastric ulcer heal during life (9). But to bring about this happy result early diagnosis is necessary in order to prevent complications, and the strictest discipline is essential, no neglect in hygiene, diet or medicine being permissible. Of prime importance is rest in bed for a period of four to six weeks with very gradual transition to active exercise, a period of rest after each meal being enforced for months after the patient is up and about. Attempts at feeding must also be tentative, as there is no general rule applicable to all cases. Starvation may be necessary for the first few days, and is usually well borne if saline enemata be administered to supply tissue loss and maintain the moderate needs of patients who are absolutely at rest. Nutrient enemata of six ounces given every six hours may next be tried, and, later on, mouth feeding commenced with small quantities of milk and lime water to which the addition of milk of magnesia may be necessary. After several days, broths and raw eggs may be added, and after four weeks finely divided albuminous foods, such as minced meats, white fish, chicken, tender beef and light potatoes. All coarse, irritating and spicy rich foods should be avoided for several weeks. The best drug is undoubtedly bismuth, the constipation of which can be overcome by combining with it light carbonate of magnesia. Silver nitrate is also highly recommended. Severe pain may require morphine or orthoform, which last drug was formerly thought to be an aid in differentiating the pain of gastralgia from that of gastric ulcer (10). Other symptoms must be met as they arise.

Although no single rule applies to all cases, certain clinicians have laid down details of methods, with which their names are identified and for which they claim the best results. Thus W. V. Leube (11) reports 547 non-hemorrhagic cases with 90 per cent. cures—the majority in from four to five weeks, and no deaths; and 90 per cent. cures with 2.50 per cent. deaths in hemorrhagic cases. His treatment is based upon four cardinal points: 1.—Rest in bed; 2.—Karlsbad water, a quarter liter, taken luke-warm; 3.—Hot poultice to epigastrium, except during hemorrhage, when ice bags are used instead; 4.—Light diet of high nutritive value and easy digestibility.

Lenhartz's method is based on the theory that ulcer is prevented from healing because of mechanical stretching of the organ, hyperacidity and anemia. He opposes the main ideas of the usual "abstinence cure" and advocates: 1.—Concentrated albuminous food continuously; 2.—Rapid increase of nourishment; 3.—Absolute rest for four weeks with ice bag for the first ten days. Senator adopts a middle course and advises glutin or gelatin for its soothing and hemostatic effect, fats for their counteracting effect on the hyperacidity and to soothe the ulcerated surface, and sugar because it is easily digested and nutritious. Later he adds eggs, chopped meat and jellies.

The above medical measures will be successful in the vast majority of cases of acute peptic ulcer, but many cases certainly fail under medical treatment. The proportion of these failures is variously estimated by different observers, the average mortality in 20 large series of cases collected and quoted by Musser being 8 per cent. (14). Surgeons, however, claim that recurrence takes place in nearly half the cases after "medical cures" (12), and that surgical interference, on the other hand, shows an ever diminishing mortality in each succeeding year. While agreeing with the medical men that rest for the stomach is the principal factor in cure, the surgeons claim that this rest can only be secured by the surgical operation of gastroenterostomy, preferably by the posterior loopless jejunal method, thus providing sufficient gastric drainage.

It is difficult to draw absolute indications for surgical interference, but any case of gastric ulcer which has resisted *rigid* adherence to the principles of rest, diet and medication for two months, should be submitted to the surgeon because such a case has become chronic and liable to the occurrence of complications, such as perforation, hemorrhage, perigastritis with adhesions or abscess, stenosis of an orifice, and constrictions caucing deformities. A case with early slight hemorrhage does not require surgical intervention, and even a single large hemorrhage does not demand operation until medical measures have failed to control it. This applies only to acute cases. A gastric ulcer which, after causing dyspeptic symptoms over a prolonged period, eventuates in hematemesis should be operated on, as the ulcer is probably an old one, the tissues are indurated, spontaneous healing is difficult, and thrombus occurs less readily. Persistent recurring hemorrhages, with short intervals between, demand operation. Perforation demands immediate operation, as every hour's delay costs the patient 8 per cent. of his chances of recovery (13). After closing the perforation, a gastroenterostomy should be performed in all cases.

Hour glass contraction and other constrictions of the stomach demand the establishment of proper drainage by suitable surgical procedure.

Conclusions—1. The crux of the diagnostic situation in stomach disorders is not the study of the stomach itself, but is the study of the individual, including his nervous system, cardiovascular system, renal and other excretions, and his entire makeup.

2. Cases of acute uncomplicated peptic ulcer need not be immediately handed over to the operating surgeon.

3. Cases of chronic, recurrent, or complicated gastric and duodenal ulcer are surgical cases.

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REPORT OF TWO CASES OF ADDISON'S DISEASE.*

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The widespread interest in Addison's disease at the present time perhaps justifies the report of two cases presenting many interesting features.

My first case is that of an Italian married woman, 39 years of age, a shopworker, who was under observation for only forty-eight hours before death. The history was that of good health until three months previous to admission to the hospital. She

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then had severe pain in the abdomen and back, which for a time became less severe, and was accompanied by sleeplessness and loss of appetite and strength. After two months her weakness became so severe as to confine her to bed; at this time she had abdominal pain, vomiting, hiccough, insomnia, constipation, and headache, and in the last three months she had lost thirty pounds in weight. Her hands and face grew darker during the last month.

While under observation the essential features which were noted clinically were pigmentation (to be described in the autopsy protocol), marked asthenia, weak pulse (B. P. 84 mm. Hg.), and signs of apical tuberculosis. She had an antemortem rise of temperature to 104.2° F., and died with pulmonary edema.

The autopsy was performed thirteen hours post mortem, and was limited to an abdominal incision, through which I was able to remove the thoracic viscera. Externally she was a well nourished woman with brownish pigmentation of the face, back of hands, lips, and gums. She presented the external features indicating status lymphaticus, with the single exception that the hair was more abundant than would be expected in this type in a woman of her age.

The gross anatomical diagnosis was: Chronic fibro-caseous tuberculosis of both adrenals; pigmentation of skin; chronic adhesive pleurisy and pericarditis; healed apical pulmonary tuberculosis; healed tuberculosis of bronchial and retroperitoneal lymph nodes; lymphoid hyperplasia of stomach and intestines; chronic parenchymatous nephritis; chronic salpingitis and ovaritis. No accessory adrenals and no thymus gland were found.

This diagnosis was supplemented microscopically as follows: Tuberculosis of thyroid (weight, 35 grams); tubercles in liver and spleen; hypertrophy of islands of Langerhans (weight of pancreas, 75 grams). The left adrenal was small and very firm, and on section none of the normal markings of the gland could be distinguished, the gland substance being completely replaced by large, white caseous masses. The right adrenal was considerably enlarged, its surface being pale and nodular. On section, there were seen few remains of the markings of the gland, the cortex being represented by faint yellowish streaks. At the lower pole was a large caseous focus, and surrounding the entire cortex, for a width greater than that of the normal gland, there was pale, firm tissue containing a few caseous foci. Microscopically, the adrenals showed complete destruction, being entirely replaced by a central caseous area surrounded by tuberculous granulation tissue, containing some tubercles and areas filled with plasma cells.

The second case was that of a Canadian farmer 34 years of age, who at three years of age had a lesion which was represented by a complete ankylosis of the left hip. He had had bronzing of the skin for eleven years, and had lost twenty-five pounds in weight in the three months previous to entrance to the hospital, where he sought admission on account of weakness, soreness of the muscles, and loss of appetite. Aside from his ankylosed hip, pigmentation (to be described later), asthenia, soreness of the muscles, and low blood pressure (85 mm. Hg.), nothing remarkable was noted clinically.

At the autopsy, which was performed two and a half days post mortem, he was found to be still well nourished, with marked bronzing of the skin of the head, face, and dorsum of the hands, and pigmentation of the lips, buccal mucosa, and glans penis. He also presented numerous symmetrically distributed, circular, macular lesions, about 7 mm. in diameter, some with pigmented margins, over the trunk and extremities, in front and behind.

The gross anatomical diagnosis was: Caseous tuberculosis of adrenal glands; chronic coxitis (tuberculous?); chronic adhesive pleurisy; chronic ossifying myositis of gluteus medius (left); hyperplasia of lymphoid tissue of lingual and pharyngeal tonsils, pharynx, larynx, spleen, and small and large intestines; congestion of lungs; status lymphaticus. No accessory adrenals were found. There was no arterial hypoplasia.

Microscopically, the adrenals showed the same complete fibro-caseous destruction. The semilunar ganglia were large and contained chromaffin: There were some small cervical nodes containing healed tuberculous areas. The pancreas weighed sixty-five grams, and showed no pathological change; nor did the thyroid, which weighed forty-five grams. The thymus, which weighed twenty-one and a half grams, showed marked hyperplastic changes. One parathyroid, which was sectioned, was found to be the seat of a very extensive fibrosis showing only small remnants of the gland embedded in the fibrous mass. This is a condition which I have not seen described elsewhere.

A third case occurring in our laboratory some time ago, and already described by Dr. Pappenheimer in connection with status lymphaticus, was that of a woman of

32 years of age, who had a typical clinical history of Addison's disease. She presented at autopsy: Diffuse bronzing of the skin; pigmentation of mucous membranes; tuberculosis of both adrenals with complete destruction of the medulla and only microscopic rests of the cortical substance; tuberculous spondylitis; general lymphoid hyperplasia; arterial hypoplasia; a ten gram thymus.

It is interesting to note that these three cases all show signs of a status lymphaticus, in view of Hedinger's published observations of seven out of fifteen cases of Addison's disease associated with status. Hart and Wiesel have also emphasized this coincidence, and Wiesel reports a case of an eighteen-year-old man who died while swimming, and who was found to have a large thymus and an hypoplasia of the chromaffin system. To the latter Wiesel ascribes his sudden death, rather than to his status lymphaticus.

As to the causation of Addison's disease, about the only generally accepted theory is that it is a disturbance in the chromaffin system, of which the adrenal is supposedly the main depot. Addison's original tenet, that tuberculosis of the adrenals covers all, has been found wanting.

Lewin in the study of 370 cases of typical Addison's disease found:

Typical cases of Addison's with sound adrenals	12 per cent.
Typical cases of Addison's with diseased adrenals	88 per cent.
Diseased adrenals without bronzing	28 per cent.
Diseased adrenals with bronzing	72 per cent.

He also mentions forty-four cases of destruction of the adrenals by various diseases in patients dying of intercurrent affections who had had no evidence of Addison's disease during life.

That even tuberculosis of the adrenals does not always cause Addison's disease is shown by numerous cases, as, for example, a case reported by Wiesel of a 16-year-old girl who had no symptoms of Addison's in spite of extensive tuberculosis of adrenals, kidney, bladder, and genitalia, and abundant chromaffin cells in the solar, suprarenal, and hypogastric plexuses, and in the ganglia along the vertebral column. Wiesel holds that Addison's disease is a disease of the chromaffin system and not of the adrenals alone; while Karakascheff holds that the disease is due to destruction of the cortex of the adrenal. He reports a case of complete destruction of the medulla by an old hemorrhage without Addison's.

At the present time these seem to be the two main views in reference to Addison's disease. Karakascheff is very strongly of the opinion that the cortex of the adrenals can not be destroyed without producing Addison's, and explains reported cases on the ground of accessory adrenals composed of cortical tissue. He also reports some interesting cases of Addison's disease following destruction of the adrenals sequent to thrombosis of the adrenal veins.

The question, to what extent the extra adrenal part of the chromaffin system can compensate for entire destruction of the adrenal part, is one difficult to settle, as the bounds of the chromaffin system are being constantly extended by different observers, and some of the parts already described are somewhat inaccessible in the ordinary autopsy dissection. Recently the heart and ovaries have been said to contain chromaffin cells. But it may perhaps be open to question also whether all of our staining reactions are really specific; that is, whether there are not some chemically similar substances which give the same reactions.

There have been several physiological methods devised for determining the presence of adrenalin.

1. The first and best known of these is that of Oliver and Schaeffer, who first described the angiotonic effects of extracts of the gland on intravenous injection.
2. Ehrmann found that the pupil of the excised frog's eye dilates in the presence of adrenalin in dilutions as high as 1 in 10,000,000.
3. Meyer's reaction is dependent upon the contraction of portions of excised vessels when subjected to adrenalin.
4. Lastly, Comessatti has described a colorimetric reaction when adrenalin and mercuric chloride are mixed in certain proportions.

Oliver and Schaeffer found the extracts of the adrenals in two cases of Addison's disease inactive as far as the blood pressure raising reaction was concerned; and in the September number of the *Archives of Internal Medicine*, Wells and Greer have shown the extracts of two hypernephromata to be inactive by the first, second, and fourth tests.

Using the method described by Wells and Greer, I made extracts of the adrenals of my second case, and found that intravenous injections of 2 c. c. produced no rise

in blood pressure in the rabbit—this being tried with each adrenal mass independently —while an extract of a healthy adrenal obtained four and one-half days' post mortem, and prepared in exactly the same way, produced a distinct sharp rise when 0.5 c. c. was injected.

To show that adrenalin if present in the caseous adrenals could not have been masked in this experiment by a possible depressor action of any of the products of caseation, I injected a rabbit intravenously with a similarly prepared extract of some caseous mesenteric glands obtained from a tuberculous infant and found no change in blood pressure produced.

Similarly, the extract of the caseous adrenals produced no dilatation of the excised frog's eye in several hours, while the healthy adrenal extract produced temporary dilatation as did adrenalin chloride in 1 in 10,000 solution.

W. H. Schultz, of the Hygienic Laboratory of the Public Health and Marine-Hospital Service, has recently said that naked eye readings of the pupil are of little value, and has devised an elaborate apparatus for observing the pupil and making accurate measurements under constant temperature and light. But I think my observations are not entirely devoid of value, as they were made simultaneously under identical conditions of temperature and light, and the independent readings of four observers coincided.

The solution of the cause of Addison's disease will probably not precede a much more accurate knowledge of the inter-relations of the various ductless glands, suggestions of which are coming from the physiologists. Falta conceives of the adrenals as being active in the mobilization of carbohydrates, which are oxidized by the pancreatic secretions, and believes that in many cases of diabetes, besides an insufficiency of the pancreas there exists a primary increase of carbohydrate mobilization by means of a hyperfunction of the chromaffin system. Thus, the adrenals and pancreas are related. The thyroids stimulate the sympathetics which form a part of the chromaffin system, and the parathyroids depress them. Thyroidectomy in dogs prevents adrenalin glycosuria and diminishes the angiotonic effect of adrenalin, while thyreoparathyroidectomy increases the glycosuria.

The relation between the hypophysis and the genital organs is well recognized, and pancreatic disturbance, manifested by diabetes, is not infrequent in acromegaly, which is probably due to a hyperfunction of the hypophysis.

In my cases there are many factors to consider. In the first, we have found destruction of the adrenals, partial thyroid destruction by tuberculosis, hyperplasia of the thymus, and hypertrophy of the islands of Langerhans. In the second case, aside from the adrenal destruction, we have the thymus and the destroyed parathyroid.

What relations, if any, these bear to one another, and their exact bearing on the clinical course, it is beyond the province of this paper to discuss.

PROTEIN METABOLISM IN ADDISON'S DISEASE.*

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Although Addison's disease is one very closely connected with a gland which must have important functions regulating metabolism, since associated with tuberculosis of this organ are general weakness, loss in weight and a marked pigmentation of the skin and the mucous membranes, nevertheless the amount of chemical work which has been done in an attempt to throw light on the process is not large.

Those investigators who have taken up the cases from the point of view of protein metabolism have in the main contented themselves with a study of the nitrogen balance, and these observations have been extended further to a simultaneous determination of the effect of the administration of adrenal gland substance on the protein breakdown.

Even here the results are not uniform, for Senator (1) believes that the physiologic effect of the gland substance in case of Addison's disease is to lead to increase in body weight and appetite and to produce a retention of nitrogen, but a slight minus balance

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in calcium. Both Kaufmann (2) and Pickhardt (3) report increased nitrogen loss during the administration of the tablets, and to-day the use of the gland in the treatment of the condition has lapsed into disfavor.

Not all the cases of Addison's disease, however, show a loss of nitrogen, for in some it will be seen that nitrogen equilibrium may be maintained on a diet which is not only low in nitrogen, but much below the average in heat units. Marchetti and Stefanelli (4), on account of the way some of the patients react with this low nitrogen and caloric diets, advance the idea that the oxidative capacity of the organism is lowered.

Some isolated observations that have been made on the urine in Addison's disease lead me to suspect that the nitrogen and carbon metabolism may be abnormal. Leva (5) reports the presence of acetic and formic acids in the urine, and taurocholic acid was also said to have been detected. Gerhardt and Reichardt also say that large amounts of fatty acids were found in the urine, and the observation regarding taurocholic acid has been confirmed by Jacoby (6) in what is admitted to be a doubtful case. Marchetti and Stefanelli and Maragliano lay considerable stress on the indicanuria, while Leva and Pickhardt, on what appear to be good grounds, criticize the view that indicanuria is a symptom due directly to disturbance of the adrenal function, and point out that the appearance of large amounts of indican in the urine is probably the effect of increased intestinal putrefaction, such as occurs in many cases with diarrhea, and diarrhea is common in this disease.

That the protein metabolism, especially the endogenous protein metabolism, is lower than usual is indicated by the estimations of Leva of the kreatinin output. This observer found the kreatinin distinctly lowered, while in a control case of icterus the excretion was normal.

With regard to the proportion in which the nitrogen and sulphur containing constituents of the urine are excreted, there is an absolute lack of information.

It is true that Varannini (7), Marchetti and Stefanelli and Leva all give the results of urea and uric acid estimations, but the methods employed can not be used to determine what the influence of the condition is on the nitrogen metabolism, so that these results will not be taken up in detail.

Report of Case.

The case we report was that of a patient in Bellevue Hospital, and for the privilege of the examination we are indebted to the courtesy of Dr. Alexander Lambert.

The abstract from the notes of the case is as follows:

Patient—M. M. male, aged 50, native of Ireland. There was no family history; no cancer or rheumatism. The patient drank beer, but seldom whiskey. He denied venereal disease.

History—The patient had had no illness up to four years before coming under observation. He had to give up work on account of weakness and shortness of breath; was unable to walk without frequent stops for breath; had attacks of dizziness, with flashes before the eyes. About this time he noted that his skin was getting dark. This was first observed on the hands and face; later on other parts of the body. About two years later, he noticed that his legs were swollen. He arose two or three times in the night to urinate. He often had attacks of palpitation, but no fainting. His appetite was always good; he never had any gastro-intestinal disturbance. For two years he had pain and stiffness of the limbs after exposure to wet and cold. His chief complaint was general weakness.

Physical Examination—The patient had a large frame, was well nourished, anemic, but did not seem to be acutely ill. The face and the upper part of the body were deeply pigmented, with lighter streaks over the upper part of the face and forehead. The thighs and legs were lighter in color. The eyes were equal and reactive; to light normal; conjunctivæ very pale. The tongue was clean and moist; the dorsal surface showed patches of dark pigmentation. This pigmentation was also seen on the inner sides of the cheeks. The neck was thick, rounded and rigid.

Thorax: percussion, negative. Breath sounds, distant and indistinct. Posteriorly, crepitant râles over each base. Heart, not enlarged. Left border percussed 10 cm. to left of median line. Action fairly regular. Sounds clear. Systolic murmur heard best in the pulmonic area. Arteries thickened. Pulse small, low tension with quick upstroke.

Abdomen: liver and spleen not enlarged.

Extremities: slight clubbing of the fingers.

The patient was quite weak, and very anemic. His appetite was always very great. Except for weakness and great hunger, he complained of nothing. His bowels were

very constipated until he was put on an oatmeal diet. The high eosinophile count which appears in the report on the blood findings remains unaccounted for. The stools were repeatedly examined for parasites and none found. Trichinosis was excluded by excising a piece of the pectoral muscle and examining for trichinæ. None were found.

TABLE 1.—BLOOD EXAMINATION.

Date.	Hemoglobin.	Erythrocytes.	Leucocytes.	Polymorphonuclear.	Small Lymphocytes.	Large Lymphocytes.	Mononuclear.	Eosinophiles.	Basophiles.
April 11.....	15	1,410,000	5000						
April 17.....	14	1,520,000	2500*	44.5	20.5	8.5	5.0	20.5	1.5
April 20.....	..	.....	4700†	47.0	19.3	10.5	4.3	19.3	0.0
April 25.....	18	1,764,000	5400‡	49.5	24.7	5.7	4.2	11.2	4.2
May 2.....	17	1,604,000	2300	52.3	22.3	8.6	3.6	10.6	2.3
May 19.....	..	.....	6600	57.0					

* Normoblast.
† Normoblast (300 cells).
‡ Myelocyte (200 cells).

Dynamometric Tests—As general weakness is considered an important feature of Addison's disease, several dynamometric tests were made on the patient during his stay in the hospital. The results are as follows: R. and L. hands. April 8, R. 29.3 K.; L. 22.6 K.; April 16, R. 33.8 K.; L. 31.6 K.; April 17, R. 38.4 K.; L. 27.1 K.; April 25, R. 29.3 K.; L. 22.6 K.

Blood Pressure—The blood pressure readings with the Janeway sphygmomanometer gave the following: April 17, R. 142; L. 138; April 25, 155; May 1, R. 116; L. 122; May 8, R. 107, L. 110; April 11 (Erlanger), Systolic, 128, Diastolic 90.

During the examination the temperature was subnormal, varying between 96 and 98 degrees. The pulse rate was between 76 and 92, and the respiration 20-24. The Calmette reaction was tried on several occasions with negative results.

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Urine—April 4: Cloudy, amber; sp. gr. 1010; albumin, very faint trace; no sugar, few leucocytes, no casts, Cammidge's reaction absent.

Feces—April 11: Light brown, semi-solid, normal odor, not fatty. Microscopic, few starch granules, many bacteria, no muscle fibers, no parasitic ova.

Blood—See Table 1.

TABLE 2.—NITROGEN, FAT CARBOHYDRATE AND CALORIC VALUE OF FOOD.

Date	Total Nitrogen.	Calories.	Fat.	Calories.	Carbohydrate.	Calories.	Total Calories.
April 29.....	16.01	410	95.8	890	293	1200	2500
April 30.....	15.51	398	88.9	825	277	1130	2353
May 1.....	15.51	398	88.1	820	277	1130	2353
May 2.....	15.51	398	89.8	835	277	1130	2368
May 3.....	15.51	398	88.9	825	277	1130	2358
May 4.....	15.51	398	88.9	825	277	1130	2358
May 5.....	15.02	385	91.4	840	246	1010	2235
May 6.....	14.22	364	84.3	785	236	968	2117
May 7.....	15.51	398	88.9	825	277	1130	2358

Diet—For the purposes of an examination of his protein metabolism, the patient was put on a diet containing the following: Eggs, 280 grams; milk, 960 c. c.; sugar, 16 grams; white bread, 130 grams; butter, 20 grams; boiled rice, 480 grams; oatmeal boiled, 900 grams; tea, 480 c. c. As the diet varied slightly from day to day, the amount of nitrogen, fat and carbohydrate are given in Table 2 with the individual and total heat units of the food. As the average weight of the patient was 72 kilos and the average caloric value of the food 2300 calories, the patient received on an average 32 calories per kilo.

The urines were collected in twenty-four hour periods, and the methods which have been used in the analysis have been given in the various papers of one of us.

Nitrogen Balance—We were unfortunately unable to collect the feces quantitatively in this case, and thus are unable to give the nitrogen and sulphur balances. An examination of the difference between the nitrogen intake and the amount excreted in the urine leads one to believe that a minus balance of nitrogen was improbable. The total nitrogen intake during the period of experiment was 138.3 grams. Of this 97.6 grams were excreted through the urine. The patient's weight at the beginning of the experiment was 66.3 kilos and at the end 65.8 kilos, a net loss of 500 grams.

Volume of Urine—As will be seen from the tables, exceptionally high volumes of urine are recorded, with a correspondingly low specific gravity. On one day only did the volume fall below 1500 c. c., and on two days over 2500 c. c. were passed On the days on which the lower volumes were excreted there is a low nitrogen output. As the patient was exceedingly difficult to control it is possible, even with the care which was taken in watching him, that some of the urine was lost. This is, to a certain extent, confirmed by the lower kreatinin elimination found on these days.

Amid Nitrogen—On this fraction of the nitrogen we are inclined to lay some special stress as representing the desamidating capacity of the organism which appears to be at fault in some conditions of toxic character. The present case represents a type of disease in which desamidation has not suffered in the least. Comparing the ratios here obtained with those found in normal individuals, it will be seen that the average, 91.7 per cent., is quite as high as that which is found in healthy persons [88.5 per cent. Shaffer (8)] and ratios higher have only been found by Schondörff and by one of us in animals receiving a large amount of meat.

Ammonia Nitrogen—Both relatively and absolutely compared with urines of normal individuals on a similar diet, the ammonia nitrogen is high. This is interesting in view of the fact that other investigators have drawn attention to the presence of unusual acid products in the urine. While these were not tested for in the present case, the fact that no acetone was found in any of the samples of urine tested probably excludes the presence of acetoacetic and beta-oxybutyric acids. Despite this fact, one must admit a very considerable degree of acidosis, not dependent on the character of the food intake. We hope at some future time to take up the study of this interesting feature of the case.

Urea Nitrogen—Although the ammonia ratio is so much beyond that found in normal individuals, the high amid nitrogen ratio allows the urea ratio still to be quite within normal limits. The average for the entire series of analyses is 83.3 per cent., while Shaffer found for a similar diet 84.3 per cent. His ammonia ratio was, however, 4.3 per cent. against our 8.3 per cent.

Kreatinin—As an index of the total endogenous metabolism, it was of considerable importance to determine what the output of kreatinin was. As will be seen from the comparison with the normal figures the kreatinin is low. The patient weighed 72 kilos. The average output of kreatinin nitrogen during the time of examination was 0.32 grams. Per kilo body weight this gives a "kreatinin nitrogen coefficient" of $0.32 \div 72 = 4.4$. Even with the highest output kreatinin nitrogen, viz., 0.384 grams, the coefficient is still considerably below that which Shaffer considers normal. The coefficient in Shaffer's normal cases ranges from 11.7 to 5.4. Hence, in Addison's disease, a condition usually associated with a considerable degree of muscular weakness, the coefficient, as one might be led to expect from Shaffer's results, is low, and compares with what this observer found in diabetes and similar affections.

Kreatin—The question of the presence or absence of kreatin from the urine has seemed to one of us from results which he has obtained to be of very considerable pathologic importance. Its presence in the urine is associated by some investigators invariably with loss of body protein, although this is assuredly not always the case. Others attribute its execretion to an impaired function of the liver. In any case, its appearance in the urine, when the factor of starvation can be successfully eliminated, is probably of pathologic significance. In this case, as will be seen from the tables, kreatin is absent from the urine, and in the experience of one of us, it is the first important disease, associated with general weakness, in which no kreatin has been

found. More information regarding the behavior of other cases of Addison's disease in this particular is earnestly desired.

Uric Acid Nitrogen—On comparison with the data obtained from normal subjects, the uric acid nitrogen appears to be distinctly low, and this is especially the case towards the end of the experiment, when on one day only 0.018 grams were excreted. As an index of endogenous metabolism this corresponds with what was found in the kreatin excretion. It is worthy of note that the low uric acid excretion is found on that day on which the lowest kreatinin output was observed. These results do not correspond with those of Marchetti and Stefanelli, who obtained on some days as much as a gram of uric acid, corresponding roughly to 0.3 grams of uric acid nitrogen.

Table 3.—Nitrogen and Sulphur Partition in Addison's Disease.

Date Received.	Volume. C.c.	Specific Gravity.	Total Nitrogen. Gms.	Gross Urea. Nitrogen. Gms.	Amid Nitrogen. Gms.	Urea Nitrogen. Gms.	Kreatinin. Nitrogen. Gms.	Uric Acid. Nitrogen. Gms.	Rest Nitrogen. Gms.	Gr. Urea. Per cent.	Ammonia. Per cent.	Urea. Per cent.	Kreatinin.
April 30, '08....	2045	1007	11.220	10,210	0.916	9.294	0.382	0.074	0.554	91.00	8.17	82.83	3.41
May 1, '08....	2170	1007	12.484	11.320	1.138	10.182	0.384	0.074	0.702	90.70	9.15	81.55	3.08
May 2, '08....	1890	1008	9.090	8.320	0.800	7.520	0.274	0.060	0.436	91.50	8.80	82.70	3.01
May 3, '08....	2510	1008	11.780	10.820	0.980	9.840	0.340	0.083	0.537	91.90	8.38	83.52	2.89
May 4, '08....	2530	1008	11.740	10.728	0.860	9.868	0.329	0.056	0.627	91.38	7.32	84.06	2.80
May 5, '08....	2280	1007	11.628	10.579	0.889	9.690	0.315	0.059	0.675	90.96	7.65	83.31	2.71
May 6, '08....	1800	1008	10.980	10.135	0.918	9.217	0.333	0.032	0.480	92.28	8.36	83.92	3.03
May 7, '08....	1360	1010	8.230	7.655	0.691	6.964	0.258	0.018	0.299	93.00	8.40	84.60	3.13
May 8, '08....	1930	1009	10.500	9.726	0.965	8.761	0.310	0.027	0.437	92.65	9.23	83.42	2.95

Rest Nitrogen—The absolute amount of rest nitrogen corresponds closely with what has been found in normal urines. The ratio moreover is not only within the normal limits, but is even below the values usually obtained.

The Partition of Sulphur.

Total Sulphur—The impression which one obtains from an examination of the excretion of total sulphur is that it is high, and this is confirmed when one considers the relation which this component of the urine bears to the total nitrogen output. Shaffer's last determinations of the values in normal individuals give a ratio of 7.2. In this series of analyses the ratio is more than 1 per cent. higher. While this is perhaps not of pathologic significance, one often sees in cases with the pathologic destruction of protein that apparently a type of protein is katabolized which is high in sulphur.

Table 3.—Nitrogen and Sulphur Partition in Addison's Disease—*Continued.*

Date Received.	Uric Acid. Per cent.	Rest Nitrogen. Per cent.	Total Sulphur. Gms.	Total Sulphate. Gms.	Alk. Sulphate. Gms.	Ethereal Sulphate. Gms.	Neutral Sulphur. Gms.	Total Sulphate. Per cent.	Alk. Sulphate. Per cent.	Ethereal Sulphate. Per cent.	Neutral Sulphur. Per cent.	100 Total Sulphur. Total Nitrogen.	Phosphorus. Gms.	Per cent. Gms.
April 30, '08..	0.70	5.29	1.022	0.866	0.807	0.059	0.156	84.80	79.00	5.80	15.20	9.1	1.000	0.454
May 1, '08..	0.59	5.63	1.024	0.836	0.783	0.053	0.188	81.56	76.40	5.16	18.44	8.2	1.048	0.527
May 2, '08..	0.66	4.83	0.733	0.578	0.536	0.042	0.155	78.85	73.13	5.72	21.15	8.1	0.760	0.516
May 3, '08..	0.70	4.51	0.956	0.783	0.670	0.113	0.173	81.90	70.09	11.81	18.10	8.1	1.052	0.831
May 4, '08..	0.48	5.34	1.017	0.853	0.736	0.117	0.164	83.84	72.40	11.44	16.16	8.6	0.971	0.822
May 5, '08..	0.51	5.82	0.930	0.798	0.707	0.091	0.132	85.77	75.98	9.79	14.23	8.0	1.015	0.565
May 6, '08..	0.30	4.39	0.967	0.817	0.751	0.066	0.150	84.53	77.64	6.89	15.47	8.8	0.945	0.423
May 7, '08..	0.22	3.65	0.722	0.598	0.558	0.040	0.124	82.88	77.22	5.66	17.12	8.8	0.851	0.302
May 8, '08..	0.26	4.14	0.917	0.737	0.658	0.079	0.179	80.42	71.80	8.62	19.58	8.7	1.044	0.440

All urines acid. No kreatinin. No acetone.

Sulphate Sulphur—Comparing the results here obtained with those of Folin and Shaffer in normal subjects it will be seen that the oxidation of the sulphur part of the protein molecule has proceeded in every respect like that of a normal individual. There is certainly no deficiency in oxidation in so far as the sulphur group is concerned as has been asserted by the Italian investigators of this disease.

Ethereal Sulphate Sulphur—In view of the importance which was at one time attached to the excretion of indican in Addison's disease it is interesting to examine the output of ethereal sulphur. The figures uniformly are somewhat high, especially on two days in the middle of the experiment, but an examinaton of the metaboles in normal individuals will disclose amounts of ethereal sulphur almost as high as those found here, so that one cannot assign to this any pathological importance.

Neutral Sulphur—Neither relatively nor absolutely is the neutral sulphur increased above that found in normal subjects. As the sulphur of taurocholic acid would be found in this fraction, it is unlikely that the amount of taurocholic acid in these urines would be increased as some observers have claimed.

We are indebted to Mr. Emil Osterberg for much help in performing the chemical analyses described in this paper.

Summary.

The nitrogen and sulphur metabolism in a case of Addison's disease has been examined on a purin-free diet. The desamidating capacity of the patient and his capacity to transform the sulphur of the cystin group into sulphuric acid were absolutely comparable to that of normal individuals. A considerable degree of acidosis was observed which is not accounted for by any factor which was found in this examination. The endogenous metabolism of the patient, as represented by the kreatinin and uric acid outputs was below that of normal subjects.

1. Senator: Charité-Ann., 1898, xxiii, 287.
2. Kaufmann: Zentralbl. f. Stoffwechs. u. Verdauungskr., 1901, ii, 173.
3. Pickhardt: Berl. klin. Wchnschr., 1898, xxxv, 727.
4. Marchetti and Stefanelli: Riv. crit. di clin. med., 1901, ii, 773.
5. Leva: Virchow's Arch. f. path. Anat., 1898, cxxv, 35.
6. Jacoby: Charité-Ann., 1898, xxiii, 287.
7. Varannini: Clin. med. ital., 1902, xli, 40.
8. Shaffer Am. Jour. Physiol., 1908, XXII., 445.

THE TREATMENT OF ALCOHOL AND MORPHINE ADDICTIONS.*

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When a few weeks ago I published an article describing a treatment with which one can obliterate in a few days the craving for narcotics, I little expected the widespread interest that would be aroused. The inaccuracy of the lay press was to be expected, but this has created such false ideas of cures, that when you, Mr. President, asked me to read a paper to-night on the subject of this treatment, I gladly availed myself of the opportunity.

One risks a good deal when one endeavors to prevent the recurrence of narcotic indulgence, for heretofore the reputable profession has usually left this part of medical treatment to the nostrum or quack or the commercial charlatan. One is forced to submit without redress to the publication of interviews which were never given, and one must be prepared to accept the consequent misjudgment of his confreres.

The causes of alcoholism lie within and without a man. It is often impossible to disassociate a man from his environment, and because we cannot control a man's environment, though we may control him, we frequently fail in dealing with alcoholism.

The problems of alcoholism are sociologic, moral and medical, and many have been the failures because some of the sociologic problems have been dealt with medically, or the medical problems dealt with morally. I think it will not be uninteresting

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to this audience to consider the various types of patients that come in to the alcoholic wards in a large hospital, such as Bellevue.

Twenty years ago the young men predominated more than they do to-day. The young working man and the horse car driver were frequent patients. As electricity came into commercial use the young men diminished in numbers, because a young man could no longer spree and retain his position, and the employers more and more have demanded sobriety through total abstinence among their workmen. Modern machinery has been a great source of temperance among the working classes. To-day the majority of patients are older men, the failures in life, and the derelicts of a great city.

A few years ago it interested me to study the social condition of a number of alcoholics, and among some ten thousand men it is very noticeable that the professions in which mental strain with worry and excitement and irregular hours of sleep are predominant factors, show a larger number of alcoholics than those among whom such conditions are less pronounced. Journalists, actors and physicians are thus more prone to alcoholism than lawyers, engineers and other professional men. It seems that a craving for excitement against a monotonous existence, explains the large number of clerks, book-keepers, acountants and stenographers, who are admitted. Physical exertion near fires, producing physical exhaustion, as seen in stokers, firemen, blacksmiths, and iron and brass moulders, has long been recognized as a potent factor in producing the frequent admissions of men following these occupations, into the alcoholic wards.

Stablemen, hostlers, hackmen, and teamsters of all kinds, men whose occupations vary from periods of hard work to idleness, with exposure to varying weather, form a large class in the cities who unfortunately acquire their habits of intemperance in the early and most productive years of life. More than half the large numbers belonging to these occupations who are addicted to alcohol are from five to fifteen years younger than the age at which the greatest number of those suffering from alcoholism are admitted to the hospital. Among the eight thousand women whose statistics I studied, domestic servants predominated over those working in shops and factories, and the term "housewife" covered the large number of prostitutes such as one would expect to find in the hospital service of any large city. How large this latter number is, it is impossible to say. These, in a broad sense, are factors which the hospital statistics bring out. The personal histories of the individuals, as is familiar to you all, show that the nagging worries, the disappointments and grinding wear and tear of life, are the more personal causes in the environment of each individual. In the alcoholic ward at Bellevue there is a never-ceasing flood of rounders who simply come in, are sobered up, go out again, and return. When I kept an accurate account of these patients, they averaged one-eighth of the total number. They wander between the police court, workhouse and the hospital, and they form the majority of delinquents that the police and the petty courts have to deal with. Medical treatment cannot suffice for these, and yet it is the only endeavor at present that one can make to help them. The State Charity Aid last winter brought forward a bill advocating the formation of a Board of Inebriety, with inebriate colonies to which the different drunkards and rounders could be sent under various conditions. This has been tried in Massachusetts and in Iowa and has produced excellent results, at the same time relieving the workhouse, hospitals and police courts of an enormous mass of recurring cases. Some such action as this must be taken to meet the ever-increasing throng of chronic alcoholics which crowd the hospitals. This is not a medical problem, but sociological, and must be treated as such.

The causes of periodic drinking are different from those of the ordinary alcoholic. In a recent paper by Dr. Pearce Bailey, it is well pointed out how varied these causes are. Often it is a hidden unstable mental state, which may be an expression of a genuine psychosis, or it may be a recurrent explosion which in a few cases seems to resemble epilepsy, or it may be a recurrent sexual factor, in which the desire for alcohol is simply an expression of one factor in the general explosion. A very common form of periodic drinker is the man who persists in the delusion that he can drink moderately, and after a spree, he ceases to drink for some time: then begins gradually to nibble at it; this nibbling gradually increases until he goes on the regular protracted spree: but that form of the periodic drinker comes more into the question of the personal causes within a man, than those of his environment. In dealing with most alcoholics and in the majority of those given to any form of narcotics, we are dealing with the mentally crippled and mentally defective, and hopelessly deficient mass of humanity. After the alcohol or morphine has been removed, the residuum is often worthless, and too weak to cope successfully with the problems of existence.

In a small minority, however, we find strong individuals who through mistaken ideas of stimulation, or through the endeavor to tide over some crisis, have been led

unwittingly under the spell of the narcotic craving, which demands ever-increasing doses of a given narcotic, and from which they cannot physically break away; the majority of narcotic addictees, however, are those with weak and crippled nervous systems, either inherited or acquired through an unhealthy infancy and environment. The treatment for narcotic craving is vastly more, in a broad sense, than mere medical treatment, or more than drugs can possibly overcome in any individual case.

From a purely medical standpoint, the treatment of alcoholism can be fairly divided into the treatment of the acute attack, and the endeavor to bring the patients into such a condition that they can with a clear brain consider what their future must be. The mere cessation of drinking or the tapering off of the addictee from acute or chronic alcoholism, is not sufficient to remove the desire for the narcotic which the enormous previous consumption has brought about. Many patients remain for weeks and months in some institution mentally watching the calendar and the clock for the time when they can get out and take a drink This means sooner or later the return to their former habits, and a failure of that plan of treatment. The deprivation from a narcotic does not mean an obliteration of the craving for it. This is true of any narcotic, whether of alcohol, opium, cocaine or tobacco. The treatment of the acute exacerbation of alcoholism, or of delirium tremens, is too familiar to need description here. It is the step beyond this; the endeavor to straighten out an alcoholic and keep him straight, that I desire to bring to your attention.

After many years of endeavor to find something that would get a man on his feet with a clear brain, and with the craving for narcotics removed, I have finally come upon a mixture of drugs which produce the desired effect. As I have already published, this treatment was given to me by Mr. Charles B. Towns of this city, and consists of a mixture of 15 per cent. tincture of belladonna, 2 parts, and 1 part each of the fluid extract of xanthoxylum and the fluid extract of hyoscyamus. This is termed the specific. I have already fully described this treatment in an article published in the *Journal of American Medical Association* of September 25th, under the title "The Obliteration of the Craving for Narcotics." Briefly, it is as follows:

From 6 to 8 drops of the specific are given every hour, day and night, until either the patient shows symptoms of belladonna excess, or with the cathartics about to be described, the patient has a certain characteristic stool. This specific is increased by two drops every six hours, until 14 to 16 drops are being taken; it is not increased above 16 drops. Usually an alcoholic can be given 4 C. C. pills at the same time that the specific is begun. After the specific has been given for 14 hours, a further dose of C. C. pills is given, either 2 or 4, depending upon the amount of action obtained through the use of the previous dose. If these have acted very abundantly, only two are now necessary. At the 20th hour of the specific, 2-4 more C. C. pills are given, and after these have acted, should the patient begin to show abundant green movements, an ounce of castor oil should be given, and a few hours later the characteristic thick green mucous putty-like stool will appear. Usually the specific has to be continued, and at the 32d hour 2-4 C. C. pills are again given, and a few hours later, the castor oil. The specific can then be discontinued.

Of course, in treating alcoholics, one finds in the majority of cases the necessity to stimulate them and to give them some hypnotic, but this can be done without interfering with the hourly administration of the specific. During the first 24 hours, with the older patients, or with one in the midst of his spree, there should be given whiskey in one ounce or two ounce doses, 4 or 5 times with milk. This should not be continued after the first 24 hours, and in young robust subjects, it is usually not necessary. The belladonna symptoms which would cause one to cut off the specific and wait until they have subsided before beginning again are, extreme dryness of the throat or the beginning of delirium as shown by an insistence or incisiveness of speech with the insistence on one or two ideas, or belladonna rash, or the general flushed red dryness or heat under the skin, of which they will complain. An alcoholic is more prone to react to belladonna than is the morphinist, but if they are sensitive to this drug, they will show it in the first six or eight hours of the treatment.

After patients have been through this treatment, the desire for alcohol has ceased, and for the next few days it is simply a question of feeding them, of giving them some tonic, and of seeing that they sleep at night. It is noticeable, however, that following this treatment most of the coal tar hypnotics do not act well. The best one is small doses of trional with codein, but the older drugs of chloral and of bromides act much better. A non-alcoholic tonic will soon set these patients on their feet physically, though whenever possible it is desirable that they should be placed where they can put themselves in as good physical condition as possible. We will consider later the question of prognosis as to the permanency of their abstinence.

There are many more morphinists who have unconsciously fallen under the spell of the habit through no fault of their own, than can be said of alcoholics. Often pain in sickness or the foolish prescription of some physician have been the means whereby the patient has unwittingly fallen into the habit of taking morphine; but they desire to get away from it, realizing their slavery, they grieve over it, they resent it, and they wish to be free from it. In this they differ from the alcoholic. The causes of morphinism in this country at least are more personal, more wrapped up in the individual nature, than present in the environment of a man. When it is possible to get them off their habit, they are therefore easier to deal with, although the pain and suffering which they previously endured made it infinitely more difficult to break them from indulgence in the drug even for a short time, than was true of the alcoholic, but it is just as necessary to take away the craving for morphine, as any other narcotic. To anyone who has ever tried to break off a patient by the old withdrawal methods when they were taking goodly amounts of the drug, and has struggled to keep them free from it after they have ceased taking it, the difference in the picture when undergoing the treatment by this new method, is most striking.

With this treatment most patients do not suffer more than a bearable amount of discomfort of hot flashes, slight pains, and the discomfort of their cathartics. When properly administered, this is the full extent of suffering with the majority of patients. Some do not go as far as this, a few suffer more. But when improperly administered, they can suffer as much by this method as by any other.

Briefly, in treating a morphinist, the same specific is given as I have spoken of for alcohol, beginning with from 6 to 8 drops every hour, day and night, until the characteristic stool is obtained, or until the belladonna symptoms cause one temporarily to cease. Before beginning the specific, the patients should be kept comfortable with their accustomed dose of morphine. They should be given 4 or 5 C. C. pills, and when these have acted, the specific should be begun and given every hour, day and night, beginning with 6-8 drops, and every six hours increasing two drops, until 14 or 16 drops are being taken every hour. Do not increase above 16 drops. If the patient shows the toxic action of belladonna, already spoken of, the specific should be cut off and not given again until these symptoms subside; then one should begin again with the 6-8 drops. If a patient is very sensitive to belladonna, one may have to feel one's way with 3-4-5 drops of the specific.

With the beginning of the specific, the patient should have from 2-3 to 3-4 of the total daily dose of the morphine or opium in the form in which they have been taking it, and in the manner in which it has been taken, either by mouth or by hypodermic, either morphine or opium, laudanum or paregoric. This should be given in three divided doses at half-hour intervals. After 14 hours the patient should be given 4 C. C. pills with 5 grains of blue mass or some other form of vigorous cathartic, such as the vegetable cathartic pills of the Pharmacopeia with ginger and capsicum and a 25th of a drop of Croton oil to each pill. These I have called B. B. pills, for short. Either 4 or 5 C. C. pills with blue mass, or 4 or 5 B. B. pills, should be given at this 14th hour. After the 20th hour of the specific, the patient should have 4 or 5 B. B. pills and blue mass, and if these do not quickly act they should be followed by 4 or 5 C. C. pills, and then an ounce of Epsom salts or Hunyadi water every half hour for 4 or 5 doses. If in an hour or two these do not act, 4 or 5 more B. B. pills followed by the salts should be persisted in until the bowels do act. This sounds extraordinary, but the difficulty with which one obtains a cathartic action at this time in some morphine patients, is beyond belief. The ordinary withdrawal diarrhea as seen in the old treatment of morphine, does not occur here, but on the contrary at this time there is a most persistent constipation that is only overcome with the greatest difficulty. If at this time of the 20th hour the cathartics do not act, the withdrawal symptoms of sneezing, nervousness and pain come on in full force, and the patient begins to suffer intensely. If the cathartics do act well, a second dose of morphine or opium should be given, of about 1-3 or 1-6 of what was given as the initial dose at the beginning of the treatment. Twelve hours after this second dose of morphine or opium, the patient should again have 4 B. B. pills, or 4 C. C. pills with 5 grains of blue mass, and following this the stools will begin to be green. Often at this time they have large liquid green stools, but these are not the characteristic green stool spoken of. After the liquid green stools have occurred, following the 32d hour cathartic, an ounce of castor oil disguised in coffee or orange juice, but not in whiskey, should be given, and the thick green stool is obtained in a short time.

When the patients have had this characteristic stool, some of them will feel suddenly relaxed and comfortable, where previous to this they had been nervous and uncomfortable. If just before the castor oil acts they are very uncomfortable, one

should not hesitate to give them 3 to 5 grains of codeinphosphate, which will make them comfortable and not tie up the secretions as morphine does.

After the characteristic stool has been obtained, and the specific has been stopped, some patients are still nervous and upset. Sometimes a high saline enema will remove all this, and the patient will become relaxed and go to sleep. Others will wake up after the codein and be comfortable and with no further desire for the morphine. In fact, their desire for morphine has disappeared.

At the 30th hour of treating a morphine patient, and if in a weak condition at an earlier hour, one must begin stimulating with strychnine, a 60th to a 30th of a grain.

In treating patients suffering from cocainism combined with morphinism, one must stimulate with strychnine early, and it is not necessary to give any initial dose of cocaine, but with these patients, one must never fail to remember that cocaine has been used as a strong antidote against the morphine, and the initial dose of morphine must be smaller than when taken alone, and should never exceed half the amount taken in 24 hours. When treating a patient who is addicted to cocaine alone, one should give the heart stimulants early, and it is not necessary to give any of the cocaine to begin with. The cocaine patient sleeps heavily through the first 24 hours of his treatment, and is aroused with difficulty to take his specific. These patients, after they have had the desire for morphine or cocaine removed, rapidly improve. Their appetite improves with equal rapidity, and they gain flesh fast and build up very quickly.

Now, considering all morphinists and cocainists and alcoholics, after one has obliterated the craving for their narcotic, what is the prognosis in regard to the patient returning to his addiction? I have no absolute figures as yet, because it is impossible to tell at this time what proportion of the number treated have relapsed. Most morphinists desire to stop their addiction, and earnestly and honestly wish to be free from it. If relieved of the craving for their narcotic, and if free from this desire for 48 hours, they can readily stay free without effort for as many years. It is only when the cause which first brought them to the addiction again becomes active, whether it is plain insomnia, sorrow, worry or discouragement, that they are prone to relapse. The majority of morphinists become addicted to its use unintentionally, and in my experience, after watching the effects of this treatment for five years, the vast majority do not relapse. From the cases which I have seen, I believe that 85 per cent. have stayed off their drug. This number is only a mental estimate of my own. I have not figures to prove it. It is, however, my present belief.

With cocainists, the causes which led to the addiction are more seductive, and more apt to become re-operative, and therefore the patient is more prone to relapse. If within a year after one has removed the craving for this drug, the patient becomes mentally or physically exhausted, he is exceedingly apt to return to his addiction, but if after that time he is kept in good physical condition, and not permitted to become overexhausted, the majority of these patients do not relapse.

With alcoholics the question is different, and among these it is especially necessary that there should be an honest, deep-rooted desire on the part of the patient to be free from the habit, and a full frank acknowledgment that he cannot ever indulge in a single drink of alcohol in any form without danger of a relapse. If a patient realizes this fully, and acknowledges it to himself, that he is not as strong as he thinks other men are, and that he is one of the men who cannot take this narcotic in moderation, and is one of the sensitive human beings to whom a single drink is the sure beginning of a prolonged debauch, you have gone a long way in helping that man to a permanency of abstinence.

Most alcoholics do not desire to stop drinking. Most of them are unwilling to acknowledge that they cannot drink even in moderation. They possess an abnormal self-conceit, through the density of which it is almost impossible to drive in the ideas necessary to make them realize the danger of a single indulgence.

Each form of periodic drinking has to be treated by itself, and the causation of periodicity unravelled and worked out. Even with these patients, I have seen this treatment straighten them out, and bring them to a realization that they could not drink at all.

You have noticed that in this paper up to this time, I have not used the word "cure." This has been a deliberate omission. To cure a man of the alcohol habit, or of morphine or cocaine by means of drugs, would be to give him something that would in some way prevent them from ever indulging in their narcotic again. This would be to guarantee the future acts and environment of another individual, and no wise man would ever attempt to do such a thing. We cannot rebuild a weak character by means of drugs. We can by long training and moral influences accomplish this result, and it is for this reason that in the past, where it is possible, it has been

a very noticeable fact, that those patients who could be religiously influenced are those in whom we have found the strongest incentives to refrain from narcotic addiction. We have no drugs to follow the daily life and daily walk of an individual, and act as a chaperone to keep him from narcotic indulgence. This treatment does not offer such a safeguard, and when the word "cure" has been misquoted in connection with it, I, for one, have not been responsible for it.

If we can obliterate the desire of a man to reinduige in his narcotic, we certainly have put him in a position where he can take a mental account of stock, and consider whether it is worth while to cease his indulgence, or whether he desires to go on again. He can then, with a clear mind, consider what portion of his environment is dangerous to him, and thus see clearly what it is he has to avoid in future. He can see clearly where he has been in error in his habits of life, or as I have said, in his environment, and can re-construct his habits of living, and thus make what started as the obliteration of his craving for narcotics, into a permanent abstinence from his indulgence. Medically, it does not seem that it is possible to do more than this. By medically, I mean treatment with drugs. Morally, if one possesses the confidence of one's patients, and can influence them and make a deep impression on their minds when they are in the full reaction following the cessation of their narcotic poisoning, one may make a lasting impression which will be of inestimable value to the patient. In this way one may help to bring about a cure.

All these narcotic addictees, after their treatment has obliterated their craving, are still not robust people in the full vigor of their faculties. They require physical care, and they require mental help. It is hard for many of them to believe that in so short a time as from 3 to 5 days they can be absolutely free from all desire to indulge again, and many of them require some days to regain their self-confidence, but this soon returns.

This treatment, gentlemen, has been offered to the profession with the earnest desire that others would try it and prove its value. In my hands it has obliterated the craving for narcotics, but that, as many of you realize, is but the beginning of the regeneration and cure of the patient. It is my belief that it is a step in advance of any form of treatment which has yet come within my knowledge. It is, however, necessary to follow out the many details which have been laid down in my first article, and mentioned briefly in this paper, in order to make this treatment a success.

If it is not properly carried out it does not attain its object, and the patient is left in a disappointed, miserable frame of mind. The craving is not obliterated, and it is a woeful failure. If carried out accurately, I feel confident that you will succeed as well as I have, and will have the satisfaction of breaking up many a narcotic addiction with which formerly you had struggled only to be forced to acknowledge to yourself the bitterness of defeat.

NORWAY FOR NEURASTHENIA.*

CHARLES E. NAMMACK, M.D., LL.D.

When that much quoted individual "the overworked business man" makes a trip to Europe in search of rest and recreation, he usually looks for it in such busy marts of commerce and pleasure as London, Paris, Berlin, and Vienna. These have their vantage points for study of their industrial, social, æsthetic, sanitary, and moral conditions, and usually leave the American with the pleasant satisfaction that our own large cities compare very favorably with them in similar respects. But for one who can spare three weeks from his itinerary, for something more restful and inspiring, a visit to Norway can be heartily commended. The number of touring steamers now leaving the various parts of England, Scotland, Holland, and Germany, make the necessary connections easily available, and the Norway trip is well worth while. A direct trip from New York to Christiania can also be made by comfortable steamships.

Norway consists of one huge mountain mass cut through in all directions by valleys, gorges, and passes, intersected again by lakes and rivers forming torrents, cataracts and waterfalls innumerable, while the coast is indented by deep fjords

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which penetrate the land in many cases for a hundred miles and upward. The coast is surrounded by a skjaergaard—a barrier of innumerable islands and rocks forming a natural breakwater between the sea and the mainland which, with but a few short breaks, makes a perfectly smooth and navigable channel.

Norway lies between 57° 58′ and 71° 11′ north latitude, its length being about 1,200 miles, and naturally must present some varieties of climate. But these modifications are not due so much to difference in geographical position as to other operating causes, such as vicinity to the ocean, height above the level of the sea, peculiarly sheltered situations, and a variety of other causes. The western coast, particularly at its northern part, enjoys a particularly mild climate owing to the fact that the Gulf Stream impinges upon it at about latitude 62°. Thus the mean temperature at the North Cape and at Christiania during the winter months is the same, although these places are separated from each other by 12° of latitude. But in the interior, out of the influence of the sea air, the cold in winter is intense and the heat in summer is equally oppressive. Thus at Valle, latitude 59°, altitude 1,000 feet, the thermometer in summer may stand at + 42° C., and in winter fall to—35° C. But, on the whole, Norway enjoys the mildest climate of any region so remote from the equator. Around the North Cape, in latitude 71° 11′ the sea never freezes except at the head of the fjords, although in the same latitude Sir John Franklin perished in North America. Owing to the continuous daylight in summer, vegetable growth goes on with incredible rapidity, and the rose embowered houses of Molde, 3° north of St. Petersburg, will remind one during July of our own lovely southern California homes. Wheat is cultivated as far north as 64.5°, rye as far as 69°, and barley and oats occur up to 70°. The annual rainfall on the western coast is heavy, but diminishes from the coast inland. At Bergen, the first port of call for the tourist steamers, it exceeds seventy-five inches. At the entrance of a fjord it may be eighty inches, but at the head of the fjord may register but sixteen inches. The traveler must not be discouraged by an arrival in the wet at Bergen, where it is sure to rain at some hour of almost every day. There is a beautiful country awaiting him far away toward the icy north, a land of magnificent mountains, wild ravines, picturesque lakes, superb glaciers, fjords reaching far inland into grand scenery, countless cascades, and rapids, rivers, and streams which plunge in splendid waterfalls from the heights into chasms. And in the northern part of this land from May 30th to August 1st, the sun shines day and night, the stars are never seen, and the moon looks pale and sheds no light upon the earth.

Once landed in Norway we are in the land of romance, and the flaxen haired, blue eyed, simple, honest men we meet carry us back to the days of the Norsemen and of the Vikings. The absence of obsequious servility, so noticeable in those who serve us in other European countries, is peculiarly grateful to the freedom loving American, and the sturdy sense of equality with which your stolkjaerre driver shakes your hand on parting compels your admiration and respect. Independence and frankness characterize all classes of society, and the absence of class lines has played a great part in the high place the Norwegian people hold in the culture history of Europe. Björnson asserts that "no other country possesses so many men in official positions (and professions) who are peasant born." The great national university at Christiania is attended by the sons and daughters of the humblest farmers.

Norway has an excellent system of district physicians and midwives for attendance upon the sick poor. Vaccination is compulsory and no child can be confirmed without producing a certificate of successful vaccination. The death rate would be very low if the drowning incident to the shipping, lumber industries, and fisheries were excluded. Acute bronchial catarrhs are among the most frequent epidemic diseases, and tuberculosis occupies the prominent place among the chronic infections. Leprosy, under the policy of segregation, is markedly decreasing, but is still so commonly seen as to excite no hysterical leprophobia.

In spite of a steady stream of emigration to the United States, the population of Norway has doubled during the past fifty years, and wise parliamentary measures to improve the economic condition of the farmers and to diminish the occupation dangers of the factory laborers, have done much to minimize the hardships of people living under unfavorable physiographic conditions. The people are industrious, phlegmatic, sober, religious, and contented, and a few weeks spent amongst them, and in sight of their everlasting hills, would be the best tonic for a restless, skeptical, neurotic invalid. Their absolute belief in the mercies of an all-wise Creator, their absolute confidence in one another, their respect for law and order, form a refreshing picture in these days of religious unbelief, social unrest, business dishonesty, and official corruption.

After the restful cruise amongst the fjords, another steamer may be taken at Trondhjem for the journey to the North Cape and for the wonderful sights of the midnight sun. Fog is apt to defeat the object of this trip at its terminal point, it being estimated that but one out of every four tourists finds the sun unobscured by fog, but no one admits disappointment, because at some time during the week occupied by this tour within the polar circle the phenomenon is sure to be observed and well repays the journey. The invaluable "Herr Baedeker" says that those who have the rare fortune to see the midnight sun in the Lyngenfjord before or after reaching North Cape witness a more beautiful scene than at North Cape. This Lyngen district will well repay a week's stop over, after the trip to the bleak and inhospitable North Cape, but the traveler who has noted the attractions of the wonderful, beautiful Hardanger Fjord on the way up, will probably make his stop over there, if time permits, after his return to Bergen. Bergen has many features of historical, and one of pathetic interest—the leper hospital, where all varieties and stages of leprosy may be studied. Since the lepers have been isolated and denied the right of marriage (1856) there has been a decrease of nearly seventy per cent. in the number of cases.

From Bergen to Christiania, the beautiful Valders route, which is a combination of railway, steamer, and carriage travel, offers wonderful scenic and human interest, the journey being broken overnight at Vossevangen which, in any other country but Norway, would be considered a beautiful town. Arriving at Christiania, the modern capital, the student of social conditions will be interested in the public control of the liquor traffic, which has done so much to control intemperance, promote health, and diminish crime in Norway. This Göteborg system, introduced about forty years ago, is practically a system of local option administered by philanthropic companies, the profits of the business going to public utilities. Norway originally consumed more alcohol per capita than any other country in Europe; to-day her annual consumption is less than that of any part of Europe except Finland, where women's suffrage has practically legislated liquor traffic out of existence. Since adopting temperance the death rate of Norway has fallen from thirty-three per 10,000 to 10.5. There is no restriction on the sale of beer, which in Norway contains 3.5 per cent. of alcohol. Christiania is a beautifully placed city and is fast becoming popular as a winter resort for those interested in such sports as skeing, sledging, skating, tobogganing, ice pegging, and the like.

THE PSYCHOPATHIC WARDS AT BELLEVUE; THEIR FUNCTIONS AND AIMS.*

By M. S. Gregory, M.D.

(Resident Alienist, Bellevue Hospital.)

So great and so widespread has been the misunderstanding of the work and scope of the psychopathic wards of Bellevue Hospital, not only among the laity but even among the medical profession, that when your president invited me to read a paper before your society, on the Functions and Aims of the Psychopathic Wards, I was pleased to avail myself of this opportunity to come before you, and I shall try, in the time allotted me, to give you a brief outline of what we are trying to do in this department of Bellevue Hospital.

Before entering, however, upon the present situation, and in order, perhaps to show you the origin of some of the misunderstandings of which I have spoken, and the later developments that have entirely done away with most of the causes for criticism, many of which were perhaps only too just, it will not be amiss to sketch very rapidly the history and development of this department.

Prior to the year 1879, there was no provision in any general hospital for the care and treatment of the mentally disordered. In his "History of Bellevue Hospital," Dr. Robert J. Carlisle tells about these patients, often most refined and educated, who were kept in the so called "alcoholic cells" in the basement of the hospital building, in the company of the city's inebriates, its cases of delirium tremens, and among its criminals. It is true that attempts were made to have these patients sent immediately to the city insane asylum, but for obvious reasons there were many delays, and thus the intolerable condition of affairs became so evident that a change had to be brought about.

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In this year, the first pavilion for the insane was erected, with the purpose, however, of merely separating those with mental diseases from the alcoholics and criminals for a few days, until the necessary steps could be taken for their transfer to the city asylum. No attempt was made to treat them; there were no facilities. There was no resident physician, and no nursing staff worthy of the name. The latter were mostly recruited from the semi-recovered alcoholic and from the inmates of the lodging houses, whose ability was commensurate with the pitifully meagre wages which they were eager to accept.

The advantages obtained in the erection of this new building were definite, but had little reference to the amelioration of the mental health of the patients. They were separated from the sordid environment of the alcoholics, but that was all; it soon became apparent that such a system could not exist, since intolerable conditions arose from the lack of constant supervision of this—for, the most part irresponsible and unreasonable class, and from the particularly unfit type of the nursing force. It was during this era that much of the ill odor attending the "insane pavilion" arose, and which gave origin to the traditional prejudice from which we still suffer.

In 1882 an advance step was made in the appointment of a resident physician. But with the old equipment, and the lack of provision for nursing, conditions did not very materially improve. There were practically no records kept of these patients during a period of fifteen years.

Notwithstanding all that experience should have shown, when in 1898 the new and present building was erected, the idea that the psychopathic wards should simply act as a transfer station to the State hospitals still seemed to be in the minds of those who planned the new wards, with the result that the accommodations provided were woefully inadequate to meet the growing demands of the increasing population. Four years later, in 1902, the Department of Bellevue and Allied Hospitals was created as a separate branch of the city administration and placed under the management of a board of trustees. A radical reorganization of the entire hospital system was undertaken by this newly appointed board of trustees, and naturally the psychopathic wards shared in the reorganization, and its development along modern lines of psychiatry was made possible. But it had to work out its own salvation under considerable difficulties. The building, although new, was totally inadequate and ill adapted for the special problem of mental diseases. The wards were uninviting and without cheer, while screens and window bars and peep holes gave a mediæval prison aspect to what should have been a modern hospital ward. The noisy and quiet patients were thrown together; bath, toilet, and office facilities were very meagre.

By the appointment of a resident physician in 1902, who lived in close touch with the wards, and two assistants who had experience in the care and treatment of the insane in the State hospital service, the patients for the first time received adequate medical attention. The old system of ex-alcoholic ward attendants and nurses was abolished, and high grade experienced nurses from the State hospital service was substituted, whose compensation, from forty to fifty dollars a month and maintenance, enabled one to choose them for their efficiency, intelligence, and sobriety. The wards were remodeled to permit a partial segregation of the noisy, the bars and wire screens were removed as far as was compatible with safety, comfortable and attractive furniture and wall decorations were added, and every attempt was made to give the ward an attractive and pleasing appearance. Belts, cuffs, camisoles, and all forms of mechanical restraint were abolished, and the indiscriminate use of narcotics was stopped. New bathing facilities and provisions for hydrotherapy, continuous baths, etc., have been added within the past two years, and plans for a new addition to the building have just been authorized which will materially increase our ward capacity and will make it possible to definitely separate the noisy from the quiet patients.

Further, female supervising nurses have been put in charge of the male ward both day and night, with most beneficial results. Thus, although still suffering from markedly cramped quarters, which compels us to pass our patients through, with great rapidity to hospitals, private sanatoria, and State hospitals, yet we have developed a true hospital ward in every sense of the word, where treatment to a limited extent, can be carried out, and the city's poor, suffering from mental disorders, can obtain some of the benefits which are meted out to their often less deserving brothers and sisters.

With such an equipment as we now actually possess, and with additions which are in progress, what can the psychopathic wards reasonably be expected to do for these thousands of patients that are coming in increasing numbers year by year? Statistics are usually wearying, so I shall only state that more patients are passing through the psychopathic wards of Bellevue Hospital every year than in any other similar institution in the world. Fully 3,200 cases a year are treated, and we must turn away at least 1,000 more.

What can we do for all these patients? For the majority we can only give care and treatment for from three to five days, until they can be transferred to the splendidly equipped and thoroughly modern State hospitals. It is hardly necessary to state that the vast majority of these patients require the immediate care and treatment which can be afforded only by a State hospital, located outside the limits of a great city. Fresh and invigorating air, ample room, freedom from overcrowding and disturbing noises, and proper employment and diversion—some of the most important factors in the treatment of the insane—can only be adequately attained in a hospital situated in the country.

While this is true, yet the value of the care and treatment which these patients receive during their short stay at the psychopathic wards, at the most acute stage of their disease, can scarcely be overestimated. We all realize the great value and desirability of proper treatment at the very onset of physical diseases, but we have been rather slow in appreciating its even greater importance with regard to mental disorders.

Unfavorable conditions and surroundings at the very beginning of a psychosis, at least in a certain proportion of cases, cause serious damage, intensify the disease, and retard recovery.

One purpose of the psychopathic wards, then, in the case of these patients, who must be transferred to the State hospitals, is to institute the proper care and treatment as early as possible, which can later be continued.

Another, perhaps even more important function and aim of the psychopathic wards, is to provide care for a class of patients which has been hitherto entirely neglected. I refer to patients whose psychoses are of such a character that they cannot be legally committed to a hospital for the insane, e. g., cases of alcoholism, hysteria, epilepsy, deliria, transitory attacks of confusion, excitement, etc. These patients can be cared for in no other place. Owing to the peculiar and disturbing character of their disease, general hospitals are reluctant to receive them, and they drift along until their malady becomes so intensified that they must inevitably come into conflict with the law, and find their way to jails, workhouses or insane asylums.

These patients can and should be saved. It is one of the most important functions of the psychopathic wards to render proper care and treatment to this class, as such treatment will frequently relieve the community of what might become an objectionable class, making them self supporting and in some instances helpful to those who are dependent upon them.

There were nearly 350 cases out of a total of 3,212 admissions to the psychopathic wards during the year 1908, which came under this class. There were fifty-five patients suffering from hysteria and hysterical psychoses; sixty epileptic mental disturbances, such as postepileptic confusion, excitement, equivalents, etc.; twenty mild depressive states; thirteen transitory attacks of confusion and excitement; thirty-seven psychoses due to, or following, infections, toxic and exhaustive disease, such as typhoid fever, influenza, rheumatism, scarlet fever, pneumonia, pulmonary tuberculosis, diabetes mellitus, uræmia, erysipelas, etc.; fifteen cases in which the mental disturbance was directly due to infection and exhaustion incident to childbirth and puerperal states; seventy-five cases of alcoholic and drug psychoses; fifteen organic diseases of the brain, such as cerebral hæmorrhage, syphilis, gummata, etc.; thirty-five of constitutional mental defect, or inferiority; and twenty-five patients suffering from mild attacks of dementia præcox. Patients of these latter two groups, namely constitutional inferiority and mild dementia præcox, although suffering from permanent mental disability, are able to get along in the community until some unusual occurrence places them out of harmony with their surroundings. These patients, under short and appropriate treatment, may often be enabled to regain their former mental equilibrium, and adjust themselves to their environment as previously. It should be borne in mind, however, that the patients above enumerated were only those who actually were admitted to the psychopathic wards. In addition, there were a great number of similar cases, of less severe type, which sought admission, and owing to our present limited facilities, had to be turned away. On the other hand, nearly 130 patients, or over six per cent. of the commitments to the State hospitals, during the past year, were suffering from psychoses of such a type that, had our accommodations permitted and had not been taxed to their utmost, they could have been treated at the psychopathic wards. They were sent to the State hospitals because there was no alternative, although it was realized that they would recover in a short time.

The cramped and overcrowded condition of the psychopathic wards, and our inability to keep these patients under treatment until they have fully recovered, suggested the establishment of a clinic for mental and nervous diseases in connection with the Out Patient Department of Bellevue Hospital. The main object of such a clinic was

to afford treatment to hundreds of patients who come to the psychopathic wards for examination, and who, owing to legal restrictions, and the mild type of their malady, are not proper cases for commitment to State hospitals. This clinic was established two years ago and has rapidly grown to large proportions. It is open every Thursday afternoon from 2 to 4. Patients, when discharged from the psychopathic wards after a treatment of several days which gives us an opportunity to closely observe their disorder, are instructed to visit the clinic weekly or less frequently, as their condition may require; they thus are enabled to receive treatment and advice, and at the same time, follow their daily vocations and support themselves and those dependent upon them.

Another purpose of this clinic is to induce relatives and friends of the patients who are suffering from mental disorders, to at once bring them to the hospital for examination and treatment. Although they evidently appreciate the necessity of hospital care for these patients, yet they seem to be unwilling to bring them to the psychopathic wards, because of the lingering prejudice which seems to be innate in the human mind against hospitals for the insane.

One of the most trying needs, at the present time, in the treatment of mental disorders, to my mind, is to be able to bring these patients under proper treatment as early as possible. Because mental and nervous diseases are insidious and gradual in their onset, and because in the beginning most of the symptoms are more or less subjective in their character, such patients do not seek relief until their malady has made considerable headway, requiring, therefore, prolonged and protracted treatment. This, I think, is largely responsible for the erroneous but prevalent idea among the laity and to some extent among physicians, that nervous and mental diseases are chronic and more or less incurable, and that little or nothing can be done for them. The fact is, however, that if these patients are brought under supervision and treatment very early they frequently respond to treatment as readily as in other diseases. One of our aims in this clinic, therefore, is to provide a place, where patients suffering from mental and nervous diseases, may at once be brought by timid and distrustful relatives, at the very inception of the disease, to the threshold of the psychopathic wards.

Moreover, a great number of patients with mild psychoses and of borderland conditions who presented themselves for treatment in this clinic suggested to us the possibility of a vast field for preventive and prophylactic work in mental and nervous diseases.

The tendency and goal of modern medicine is in the direction of the prevention of disease rather than its cure, and I think the time has come to do prophylactic work by educating the public in this branch of medicine, just as it has been done in the recent crusade against tuberculosis. Such educational work has robbed this disease of its terrors, so that consumption is no longer regarded, in the lay mind, as a uniformly fatal disease.

The most fruitful source of mental and nervous disorders is disregard of the rules of mental hygiene, concerning which the public is entirely in the dark, and to which physicians rarely attach any significance. As in the case of tuberculosis, very little can be accomplished by simply diagnosticating the disease and giving advice, unless the patients are also taught how to avoid the conditions which still exist, and which have contributed to their disorder. It is a well known fact that the mind can deteriorate by persistent morbid and unhygienic habits of thought and by reason of influences and surroundings which are not conducive of rectifying this unhealthy mode of thinking.

A mistaken idea held by a neurotic patient, with home surroundings which, unintentionally, perhaps, accentuate the condition, will be the foundation, frequently, for a very grave mental disorder. Therefore, in doing preventive work in the treatment of mental and nervous disorders, it is not enough to merely consider the individual and his mental make up, but the treatment must also include the regulation of his mental life at home and in his business surroundings. The correction of trivial misunderstandings in the family life, and the home attitude toward the patient and his illness, or a complete removal of the patient from his former surroundings, if necessary, may frequently be sufficient to prevent a serious breakdown in a neuropathic individual.

By the aid of the Social Service Department of the hospital and through the munificence of wealthy friends, who have kindly provided a special nurse for this purpose, we have been endeavoring to carry out this preventive work as far as our limited facilities have permitted. Proper cases selected from the clinic are assigned to this nurse, who investigates the home and business surroundings, and finds out under what difficulties the patient is laboring; then, under the direction of physicians,

as the exigencies of the case demand, the faulty conditions are corrected as far as possible. Results from this work have been fruitful beyond expectation. The field is vast, and the difficulties almost insurmountable, yet results have been so gratifying that they have furnished an incentive for further work along these lines.

How can the services of the psychopathic wards be utilized by the public and the medical profession? There appears to be considerable haziness as to the modus operandi of having patients admitted to the psychopathic wards. This arises from the unfortunate fact that the law assumes to dictate, not only who is insane, but the manner in which patients should be brought to the hospital for treatment.

As you all know, when patients become afflicted with mental diseases, unlike ordinary medical or surgical cases, they not infrequently fail to co-operate with efforts to bring them under treatment, but often even resist, and it is necessary to compel them to submit to treatment against their will. Consequently, the necessity of legal proceedings.

At the present time, patients may be admitted to the psychopathic wards in three different ways:

First. As voluntary patients. When a patient is quiet and orderly and willing to come to the psychopathic wards and remain there for examination, it is unnecessary to take any legal steps. Such patients may be brought to the hospital in the same way as ordinary medical and surgical cases.

Second. As prisoners. When a patient is acting in a manner which would be "disorderly in a sane person"—to quote the language of the law—and is unwilling to come to the hospital, his mind being clear enough to resent any interference with his liberty, his friends have no legal authority to bring him to the hospital against his will, and even if he were brought to the psychopathic wards, we should not have the legal right to admit and detain him. This last point must be emphasized, as patients are frequently brought to the hospital under some subterfuge, and when they reach the hospital we are expected to hold the patient against his will. In such a case we should be compelled to refuse admittance, which would only result in considerable difficulty and annoyance to the relatives as well as the patient. Whenever such a patient refuses to go to the hospital, as already intimated, it is necessary for the friends to notify a police officer, who will place him under arrest, making a technical charge of insanity against him, and bring him to the hospital, thereby complying with the legal requirements.

Third. Patients committed by a city magistrate for examination. In cases such as paranoia or similar conditions, when a patient refuses to go to the hospital, the police officer may refuse to arrest him, as the patient does not, in the presence of the officer, "act in a manner which would be disorderly in a sane person." In these cases it is necessary for the relatives to appear before a city magistrate and to submit evidence regarding the irrationality of the patient. A note from the family physician that such a patient is irrational and should, in his opinion, be committed for examination, may greatly aid in securing the warrant which the magistrate issues for the apprehension of the patient. If the magistrate, after a personal interview with the patient, is then satisfied with the evidence produced, he will commit him to the psychopathic wards for mental examination, for a period not to exceed five days. This latter is the strictly legal procedure, and should be followed when there is any dissension among the family and friends regarding the sanity of the patient or whenever there is any question of property rights.

The necessity for police interference in the transportation of the insane to the psychopathic wards, as has already been intimated, is extremely unfortunate, as it frequently excites insane patients, who as a class, are most suspicious.

Plans are under way to bring about a decided reform in the method of transferring patients to the psychopathic wards. In a short time, perhaps, we shall have a special conveyance in charge of trained nurses, who are also deputized as special officers, to transfer insane patients to the psychopathic wards. This method will eliminate the police with their uniforms and often harsh manners in the transfer of patients.

Conclusions.

Before concluding, I venture to make a few observations which have suggested themselves, as a result of my experience, for the past eight years, in the psychopathic wards of Bellevue Hospital.

First: People suspected of mental trouble should not be deceived. I have already pointed out that pretexts are used to bring patients to the psychopathic wards. Such deception intensifies their suspicions, and frequently makes the patients extremely excited and unmanageable. The idea that one should agree with their delusive fancies

and unreasonable demands in order to calm them for the moment is false. They will later discover the deceit, which will tend to fix their delusions and make them distrustful. This is a matter of daily observation in our service.

Second: A patient who has been heretofore temperate and who suddenly begins to indulge in alcoholic drinks to excess should not be regarded, neccessarily, as an alcoholic, especially if there is complaint on the part of his family that he appears to be mentally unbalanced. Inebriety may often be only the expression of an incipient psychosis, which is masked by the symptoms of drunkenness.

Third: Patients suffering from mental diseases who are restless and excited show great tolerance to sedatives, therefore larger doses should be given at the start. Frequently a patient is given an ordinary dose, which fails to quiet him, and the dose is then often repeated at short intervals. As a result of the cumulative effect of the sedative, we frequently have patients brought to the hospital in a state of toxæmia, in addition to their psychosis.

Fourth: There is greater danger of suicide in mildly depressed patients than in the severer types. It is true that, in the profoundly depressed, although the suicidal impulsions are stronger, yet, owing to their inhibition, they do not have the initiative to carry out their impulsions as readily as the mildly depressed patients, in whom the inhibition is not so marked. Patients who have attempted suicide prior to their admission to the hospital, we find, have been mostly of the mildly depressed types. Many of them had not been deemed dangerous, and had been regarded as suffering from neurasthenia.

Fifth: Patients admitted to the psychopathic wards are not by any means all sent to State hospitals, as is popularly supposed. As I have before stated, one-third of our annual admissions, over 1,000 patients, are discharged after being treated from three to five days.

Sixth: Lastly, an idea is prevalent among the laity, and, to our surprise, often among physicians as well, that once a patient comes to the psychopathic wards, there is great difficulty in securing his release. It seems almost unnecessary to state that we have no desire to keep patients, as the number is already far beyond our capacity: on the contrary, we do our utmost to avoid their commitment, and discharge them to the custody of their friends, if it can be done without any material harm to the patient or danger to the community; and I am sure that the State hospitals likewise assume the same attitude.

Misunderstandings of this character, no doubt, arise from the ignorance and prejudice on the part of the public. During the last two decades, the treatment and conditions in the institutions for the insane have made tremendous strides, so that now patients suffering from mental disorders are sure to receive most humane, intelligent, and scientific treatment.

I feel that the next great step in bettering the condition of the insane must come from the family physician, for he is the only one who can enlighten the public and eradicate the inborn prejudice against these institutions, so that the mentally sick will be brought to the hospitals before it is too late.

We are always pleased to receive visits from medical men, so that they may see the conditions as they really exist, and I assure you that you will always be welcome at the psychopathic wards of Bellevue Hospital.

THE RELATION OF THE INTERSTITIAL CELLS OF THE TESTICLE TO ITS INTERNAL SECRETION.*

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The fully differentiated adult individual presents in addition to the structural characters peculiar to the genus, species and variety, certain anatomical characters which are especially associated with the reproductive function. The distinction be-

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tween the sexes is shown not only in the possession of different germinal organs, but in the development of highly specialized mechanisms which render possible the union of ovum with spermatozoon, the nourishment and protection of the developing embryo, its expulsion when it is ripe for an independent existence. In addition, the rivalry of the males for the favor of the female has led to the acquirement of particular modifications of plumage, hair, voice and so forth.

It is a biological platitude to say that the sexual activities of all adult individuals are correlated with far-reaching modifications of structure. Since every species has its own manner of sexual life, there are manifold variations in the character of the sexual cells themselves, in the accessory conducting and copulating mechanisms, and in the more remote insignia of sex.

What is it that brings about the differentiation of the individual into one of two distinct sexual types? The first impetus towards further differentiation into male or female is undeniably given at a very early stage of development, or even perhaps determined by the original germinal cells themselves. That the sex of certain aphids and phylloxera is determined by the number of chromosomes in the spermatic cells has been demonstrated by Morgan (1) and Wilson (2). We have, of course, no cytological proof that such is the case in the vertebrates; but the not infrequent occurrence of manifold combinations of male and female characters in the same individual clearly show that the presence of ovary or testicle in the fœtus is not of itself sufficient to bring about the normal development of the other sexual characters. At most, we may say that the developing organs of the one sex exert an inhibiting influence upon the further development of the opposing sexual structures.

Although the original "determination of sex" occurs in the earliest embryonic period, it is not to be denied that the germinal organs exert a profound effect upon the body in extra-uterine life. The effects of castration have been carefully studied in many animals as well as man, and though many of the observations recorded by travelers and veterinarians are open to scientific criticism, we know that the removal of the sexual glands before the onset of sexual maturity is followed by a failure of the primary and secondary sex characters to undergo their normal differentiation. There is therefore rather an arrest of development along these special lines than a diversion of the original line of development into that of the opposite sex.

Since the removal of the sexual gland is followed by such striking modifications in the general structure of the organism, it has been assumed that the ovary or testis produces a specific substance in the nature of a hormone or internal secretion, which is responsible for the orderly development of the sex characters. The possibility that the secondary sexual modifications might be brought about indirectly through the medium of the nervous system, was eliminated by the decisive and classical experiment of Nussbaum (3), who transplanted the testicle of the frog into the dorsal lymph-sac and observed a normal development of the secondary and accessory genital organs. Similar experiments on other animals have been performed by Halban (4), Foges (5) and Guthrie (6).

The chemical nature of the substances producing these remarkable effects, is wholly unknown. It is probable that extracts of the germinal gland—more especially, the glycerine extracts, as shown by d'Arsonval (7)—have a stimulating effect upon the oxydative processes in general. Loewy and Richter (8) found that castration reduced the oxydative processes by 20 per cent. in male dogs or bitches, and that feeding of ovarian extract again restores oxydation to beyond the normal rate in either sex. This influence, therefore, is not specific, no increased oxydation could be produced in uncastrated animals. Of other direct effects comparable to the supposed normal influences of the genital organs—we have little direct experimental evidence. Bayliss and Starling (9) state that "menstruation" and heat can be produced in spaded animals by the injection of ovarian extracts, and Walker (10) has succeeded in preventing the castration atrophy of the prostate in dogs by injections of testicular extract. We have been able to find no other records of experiments in which by the feeding or injection of testicular or ovarian extracts, it has been possible to bring about a normal development of the primary and secondary sexual characters in castrated animals. On the contrary, Jentzner and Beuthner (11) found that subcutaneous injections of ovarian extract in rabbits, dogs or cows, did not prevent castration atrophy of the uterus.* Harms (12) has also recently reported some unsuccessful experi-

* In a series of unpublished experiments by Dr. Silas P. Beebe and the writer, the attempt was made to produce a premature involution of the thymus gland in kittens, by the daily injection over a period of several months of glycerine extracts of adult cat testicle. Kittens of the same litter were used as controls. Although the weight of the thymus was slightly less in the injected animals than in the controls, no definite histological lesions pointing to a specific action of the testicular extract could be produced.

ments in frogs. He found that repeated injections of ovarian or testicular tissue into the lymph-sacs of castrated frogs, did not noticeably stimulate the growth of the "Daumenschwiele" or excrescence normally developed on the forefoot at the time of copulation. This excrescence constitutes a striking secondary sexual character which does not appear in castrated animals. The positive experiments of Loewy (13), who fed capons with testicular extract and obtained a partial growth of the comb, are not convincing, as there was no microscopic proof that the castration was complete.

One must take into account, in judging the value of these negative results, that the periodic injection of variously prepared extracts of the dead organ is not necessarily a true guide to the action of that organ in the living body. Transplantation of the living tissue is far more conclusive and has already contributed much to the solution of the problem. By this means it has been proven at least, that the presence of testicular or ovarian tissue of the same species, even if transplanted into the subcutaneous tissue, is sufficient to ward off the usual castration effects. Thus, Halban (4) transplanted the ovaries of monkeys beneath the skin of the abdominal wall (auto-transplantation) and obtained a menstrual flow, which ceased upon the removal of the ovaries from their new site. Foges (5) transplanted the testicles in young cocks, and obtained a partial development of the secondary sexual characters. Guthrie (6) has reported similar conclusive experiments in hens.

The question as to what elements of the testicle are responsible for the production of the supposed internal secretion is the problem which has particularly interested morphologists. The question can by no means be considered as finally disposed of, although the trend of opinion is distinctly in favor of the interstitial cells. It is these structures and their possible relation to the development of the secondary sex characters that have particularly interested us. Before taking up the question of their functional significance, it is necessary to review briefly the more important histological work relating to the interstitial cells.

Leydig (14) in 1850 first noted that the interstitial tissue of the testis contained peculiar cellular elements, and although he gave no accurate description of these cells, they have been called after him, the "Leydig Cells." Kolliker (15) in the first edition of his text-book, published in 1854, also recorded the presence of the interstitial cells, and considered them as modified connective tissue cells. The first accurate description is given by Henle (16), who observed the presence of fat and crystals. Ludwig and Tomsa (17) in 1862 attempted to show that the interstitial cells were related to the lympathics of the testis. Boll (18) (1869) believed that the cells were related to the blood-vessels and that they entered directly into the formation of the capillaries. Waldeyer's (19) original view that the interstitial cells were akin to the plasma cells (not, however, identical with the cells of Ehrlich or the Unna plama cells) was later modified into the belief that they represented perithelial cells (1870 and 1872), Hofmeister (20) contributed the first embryologic studies of the interstitial cells. He found that they were relatively abundant in the fœtal testicle, occupying in the four months human embryo, about three-fourths of the total parenchyma; in an eight-year-old child, only about one-tenth. He noted also the increase in the number of these cells which takes place at puberty. He believed that the interstitial cells were of connective tissue origin and saw transitional forms between the fixed connective tissue cells and the interstitial cells. Mihalkowitz (21) (1874) maintained the same view as Boll—that the interstitial cells were related to the lymphatic system. Harvey (22) (1875) attempted to show that the interstitial cells were nerve cells related to the vaso-motor system. His theory was effectually controverted by Jacobson (23), who also has the credit of first describing a pathological increase in the interstitial cells of dogs, following trauma. Nussbaum (24) (1880) established the presence of the interstitial cells as a constant constituent of the testis, in mammals, birds and reptiles. Embryologically, he derived them from Pfluger's cell columns as cells persisting in an undifferentiated condition. He also erroneously believed that each group of interstitial cells was enclosed in a connective tissue membrane. Van Hansemann (25) (1895) made the interesting observation that the interstitial cells disappeared during hibernation, to reappear when the testicle became functionally active.* He therefore concluded that the interstitial cells bore a direct relation to spermatogenesis. Von Bardeleben (26) (1897) attempted to show that the interstitial cells were epithlial in nature and related to the Sertoli cells, and that they migrated through the basement membrane into the tubules and subsequently degenerated. These views were refuted by Beissner (27) (1898) who proved that the

* Champney has recently confirmed this observation for Rana esculenta. (Comptes rendues de l'Acad. des Sciences; t. 64, 1908, p. 895.)

Sertoli cells undoubtedly originate within the tubules. Plato (28) (1897) in his efforts to establish a trophic function for the interstitial cells, described clefts and fissures in the basement membrane of the tubules through which fat globules pass from the interstitial coils in the Sertoli cells. Beissner and later Thaler (29), to whom we owe a most careful study of the fats and lipoid substances of the testicle, totally failed to confirm Plato's observations. Thaler and Kasai (30) have made systematic studies of the life history of the interstitial cells, from fœtal life into senescence. They have shown that these elements are extremely abundant during the fourth and fifth months of fœtal life, and that after birth they rapidly diminish in number and are not much in evidence until the time of puberty, when they undergo a renewal of growth. Mitoses, however, are rarely if ever, observed. During middle life they remain approximately constant, according to Thaler, or diminish somewhat in numbers according to Kasai. Both pigment and fat gradually increase. The presence of fat in the interstitial cells, of interest in connection with their supposed trophic function [von Lenhossek (31), von Hansemann, Plato, Regaud (32)] is to be regarded as purely physiological. Though present in small quantity at birth and during childhood, the fat does not become abundant until the time of puberty. Throughout adult life it remains as a constant feature of the interstitial cells. The fat in the interstitial cells is uninfluenced by the general nutrition and by pathlogical processes. There appears to be no direct relation between the fat in the interstitial cells and that within the tubules. Thaler has pointed out morphological differences between the fat which is intratubular and that contained within the interstitial cells. Our own observations are fully in accord with his. Whereas the Sertoli cells contain fat globules which in osmic acid preparations frequently have a foamy or vacuolated appearance, or are blackened only at the periphery, the fat of the interstitial cells is invariably in the form of massive, diffusely blackened globules. This would strongly suggest chemical differences in the nature of the fatty substances and would argue against a direct infiltration of fat globules from the interstitial cells into the tubules.

The large crystalloid bodies of unknown chemical composition which are found as inclusions within the interstitial cells of the normal testicle, were first described by Reinke (33) (1895), subsequently studied by Lubarsch (34), and since have been noted by all writers upon the histology of the interstitial cells. They are found only in comparatively fresh material. Their significance is obscure.

From the above brief review which makes no pretension of completely covering the very abundant literature concerning these structures, it will be seen that there has been great variance of opinion, not only as to the function of the interstitial cells, but as to their origin. By some of the earlier writers, [Nussbaum (24), Hofmeister (20), Gaufini (35)] they are considered to be epithelial in nature; by others, to be related to the blood-vessels [Boll (18)], or to the lymphatic channels [Ludwig and Tomsa (17)]. By other investigators, and they comprise the greater number [Leydig (14), Kolliker (15), Messing (36), von Hansemann (25), and others] they are derived from the connective tissue, and represent peculiarly modified connective tissue elements. This is the prevailing view and the one to which the writers on the basis of their own studies would subscribe.

Little is known of pathological processes affecting the interstitial cells. There have been reported a number of cases showing a striking hyperplasia of the interstitial cells; this may be so extreme as to lead to the formation of macroscopic tumors. Von Hansemann (25) first observed on overgrowth of the interstitial cells in a case of pernicious anemia, and another of hemochromatosis. Cordes (37) described a distinct increase in the Zwischen-zellen in seven of fourteen cases of chronic pulmonary tuberculosis. It is, however, in the ectopic testicle that the increase in the number of the interstitial cells has aroused interest, and we have a number of elaborate studies dealing with their presence in increased numbers in cases of cryptorchidism. Among the writers who have particularly observed this are Pick (38), Felizet and Branca (39), Cuneo and Lacène (40), Ancel and Bouin (41), Dürck (42), Hanes (43), and Simmonds (44). The increase in the interstitial cells, as well as the absence of normal spermatogenesis, would seem to be a characteristic feature of the ectopic testicle.

The possibility that some of the tumors of the testicle described as carcinoma or alveolar sarcoma, might in reality take their origin from the interstitial cells, was first suggested by von Hansemann (25). Cases interpreted as Zwischen-zellen tumors have been reported by Chevassu (45) and Kauffman (46).

Our own study of the interstitial cells is based upon a series of sixty testicles, taken from subjects ranging from infancy to the seventh decade. A short analysis of our findings may be of interest, although we have little new to add to the observations of previous workers, especially those of Thaler and Kasai. As regards the number

of the interstitial cells, we have found with previous investigators, that they are relatively abundant during the fourth and fifth months of fœtal life, diminishing towards the end of gestation. In infancy and childhood, they are scant in number, and with difficulty distinguishable from the fusiform connective tissue cells which form the bulk of the intertubular substance. With the onset of puberty, the interstitial cells again become prominent, and are easily recognized by their typical form and arrangement. Throughout adult life, we have found great individual variation in the number of interstitial cells, so that it has been impossible to determine either a definite increase or a decided diminution with advancing age. Thus of cases over 15 years (not including two cases of extreme hyperplasia described below) the interstitial cells were extremely numerous in 7 cases; numerous in 10 cases; moderate in number in 23 cases; scarce in 9 cases, and in 1 case only entirely wanting.* That there is no fixed relation between age and the number of interstitial cells—at least, in adult life—is shown by group I, in which the ages ranged from 22 to 60 years.

We have likewise failed to find any relation between the interstitial cells and the presence of spermatogenesis. As this has been the observation of all previous workers, with the possible exception of von Hansemann (25) and Kyrle (47) the statement needs no further comment.

The fat within the interstitial cells, scant during infancy and childhood, gradually increases from the time of puberty. There is wide variation in individual instances however, and no apparent relation to the general nutrition of the subject.

The *pigment* does not become abundant until after puberty, and increases progressively in later life. We have never observed typical pigment in the child's testicle; however, in young infants, we have several times noted large clumps of yellowish brown pigment, lying either within the connective tissue cells or extra-cellularly. This pigment fails to give the iron reaction with potassium ferro-cyanide and HCl; treated for 24 hours with dilute Giemsa solution, after the method of Schmorl (48) for the demonstration of the chromaffin pigment, it fails to take the characteristic greenish color. Simonds (49) has recently called attention to the frequent occurrence of pigment in the testicles of young infants, due to traumatic hemorrhages at birth.

The pigment of the interstitial cells in the fresh state, has a pale yellowish brown color, which is intensified by fixation in chrome salts. With Schmorl's method, the pigment takes the characteristic bluish-green color, in this respect being identical with the chromaffin pigment. An aqueous extract of testicle containing abundant pigment, failed to give a positive reaction for adrenalin with Comessati's (50) reagent [1-10,000 $HgCl_2$]. Further efforts to identify the pigment of the interstitial cell with the chromaffin substance, have not been made, and we have had no opportunity to try the physiological reactions.

The typical crystalloids, first described by Reinke, have been found only three times in our series—probably because the material was not obtained sufficiently soon after death.

In order to decide the question as to which elements of the testicle produce the internal secretion, it is essential that we should be able to eliminate at will, any one of the three sets of structural elements which may be considered as possible claimants: First, the spermatic epithelium proper, including the spermatocytes, the spermatogonia, the spermatids and the spermatozoa. Second, the supporting syncytium, or Sertoli cells; Third, the interstitial cells or "Zwischen-zellen."

Of these three constituent elements, the spermatic epithelium is most readily eliminated. Atrophy of the spermatocytes and their descendants may be produced in various ways. Ligature of the vas deferens, as practiced by Ancel and Bouin (51) among others, is followed after a time by complete atrophy of the spermatic elements, leaving the Sertoli cells and the interstitial cells intact. Practically the same effect is brought about by exposure to the X-rays. [Herxheimer and Hoffman (52).] Furthermore, the examination of cryptorchid testicles both in man and animals [Cuneo and Lecène (40), Felizet and Branca (39), Pick (38), von Hansemann (25), Ancel and Bouin (41)], reveals as the most common finding, a complete failure of the spermatic epithelium to undergo its usual differentiation, the atrophic tubules being lined with an indifferent epithelium representing probably the Sertoli syncytium. The interstitial cells on the other hand, are not only regularly present in these cases, but are often markedly hyperplastic, as compared with normal testicles. The same condition apparently may occur in case of simple testicular atrophy or agenesia, without cryptorchidism (see below), or in atrophy following inflammatory conditions in the epididymis or in the testicle itself. Finally there are several interesting cases of

* Unfortunately, only one of the testicles from this case was examined, so that no certain conclusion can be drawn.

pseudo-hemaphroditism on record in which the examination of the male sexual gland showed atrophy of the seminal epithilium associated with hyperplasia of the interstitial cells [Abel (53), Strœbe (54), etc.].

In the majority of these cases where the reproductive cells proper are wanting, and only the Sertoli cells and the "Zwischensubstanz" need be considered as factors, the development of the sexual characters, primary or secondary, takes place normally. The experiments of Tandler and Gross (55) are particularly instructive in eliminating the influence of the spermatic epithelium itself. Whereas in castrated stags, the antlers regularly failed to develop, development of this striking secondary sexual character took place normally in those animals in which the spermatic epithelium had been destroyed by repeated exposure to X-rays leaving only Sertoli cells and interstitial substance.

The fact, borne out by a mass of evidence which the limits of this paper do not permit us to analyze in detail, seems to eliminate sharply from consideration, the spermatic epithelium as producers of the internal secretion. The problem is, therefore, narrowed down to either the Sertoli cells, or the interstitial cells, and at present we have no method of artificially separating these elements. Until such a method shall have been evolved, the final adjudication of the claim must be deferred.

There is, however, a certain class of cases which in a negative way, may be of value. If in any particular instance, the secondary sexual characters are imperfectly developed, and a careful examination of the testis shows the presence of interstitial cells in abundance, it would seem proven that the mere presence of these elements is not sufficient to bring about the development of the sexual characters. The objection that the mere presence of the cells is not sufficient to establish their functional utility, may be raised. It is true that we have to rely upon purely morphological criteria to determine whether these cells are actively secreting or not, and that we have no physiological tests to prove their functional efficacy. The objection is, therefore, valid; on the other hand, there is little reason to suppose that cells which show the same striking histological characters, as the normal cells, including the characteristic elaboration of fat and pigment, should not be equally potent to fulfill their specific function in the organism.

The following observation, has a distinct bearing upon the question at issue, and is therefore cited in considerable detail:

Case I—Acc. No. 2,371. Male, 40 years of age. No previous history could be obtained bearing upon the occurrence of inflammatory conditions in the testicle.

The general appearance of the subject as described in the autopsy protocol, was as follows:

The body is slightly above the average stature. The skin is extremely smooth and of the fine texture. There is a scant, straggling growth of hair limited to the chin and upper lip. The pubic hair is sharply confined to the prominent Mons Veneris, and the individual hairs are long and far apart. There is complete absence of hair over thorax and axilla, and over all other parts of the body with the exception of a few straggling hairs over the crests of the tibiæ. The thighs are very broad and rounded in the upper portion, tapering to the knees. The arms also, are unusually plump and round. The neck is short, the shoulders sloping. The hands and feet are small and delicately formed. The face has a puffy, somewhat vacant appearance. The subcutaneous fat is everywhere abundant. There is an unusually large thymic fat pad, showing, however, no traces of glandular structure on cross section. The aorta is atheromatous and diffusely dilated in its upper portion, but unusually smooth, thin-walled and elastic in its abdominal section. The solitary follicles of the small and large intestine are about the size of small bird-shot and prominent above the surface. The Peyers plaques are not enlarged. The adrenals are small and flat, the cortex relatively narrow.

Genital Organs—The penis is short and of small calibre, the glans very pointed. The testicles lie within the normal scrotum, but are much reduced in size, measuring 1.9x1.5 cm. and 1.9x1.4 cm. on section. The surface of the cut section is brownish, smooth and does not show the normal stringy structure. The accessory genital organs were not carefully examined.

Anatomical Diagnosis—Fatty cirrhosis of liver, sclerosis of aortic cusps, atheroma of aorta, hypoplasia of testicles and penis, juvenile habitus.

Microscopic Examination—The testicle is covered by a broad tunica consisting of rather dense laminated fibrous tissue. In the sections which were taken from several different portions of the testicle, all trace of normal testicular tissue is lost. The tubular structure ,however, is indicated by the greatly thickened membrana propria, which is composed of two sharply differentiated zones. The outer zone, comprising about one-fifth of the diameter of the tubule, stains intensely with eosin, and under

the high power, is seen to be formed of rather thick, concentrically laminated collaginous fibrils. The lighter central portion is formed of an irregular meshwork of more delicate, irregularly disposed fibrils.

A few groups of tubules contain in their central portion small masses of epithelial cells, the nuclei of which are round, well stained and show distinct nucleoli. There is absolutely no differentiation into the various spermatic elements.

Because of the preservation of the tissue in alcohol the presence of fat within the tubules could not be demonstrated.

The fibrous remains of the tubules are separated by abundant connective tissue, which is most cellular about the tubule where the cells show a concentric arrangement. No inflammatory changes are present.

The blood vessels, more especially the smaller arteries, are the seat of hyaline degeneration, affecting the inner portion of the media. The lumen of the vessels is not compromised thereby, nor are all the vessels affected. There are no thrombi.

The interstitial cells themselves are readily seen with the low power, being disposed in more or less compact strands or islands, some of the larger masses attain a considerable size so as to be visible to the naked eye in the section as dark red spots. Under the high power the interstitial cells have very indefinite outlines and in many places appear to fuse with one another. The individual cells are about the size of liver cells; the nuclei are large, irregularly oval, with a very distinct, deeply staining nuclear membrane and a poorly marked nuclear network. The nucleoli, of which there are one or two to each cell, stain distinctly. The cytoplasm takes the eosin rather intensely. There is no sharp distinction between exo- and endoplasm. The protoplasm is granular and vacuolated, the cell confines extremely indistinct. Some, but not all, of the cell groups contain finely granular brownish pigment, which in individual cells may be so abundant as to compress the nucleus into a pycnotic crescent. In sections stained for 24 hours in dilute Giemsa solution after the method of Schmorl, the pigment takes a greenish-blue color. Irregular clumps of pigment are also found lying free between the cells and suggesting that some of the cells have undergone complete pigmentary degeneration.

In one of the sections examined there is found an island of interstitial cells which in its general structure somewhat resembles parathyroid tissue. The cells themselves are well preserved, have a distinct polygonal outline, and are closely packed. The pigment is very abundant, but is not uniformly distributed throughout all the cells, some of them containing no pigment at all. A medium-sized artery enters the island at its periphery and many thin-walled capillaries ramify through it.

The sections include a number of the tubuli recti, which in striking contrast to the convoluted tubes, are lined with well preserved layers of high cylindrical ciliated epithelium. The significance of this we shall discuss presently.

The interest in this case lies in the association of a distinct hypoplasia of the sexual characters with hyperplasia of the interstitial cells of the testicle. The adiposity, the juvenile configuration of the body, the sparsity and a typical distribution of the hairs, and especially the small penis, must be interpreted as signs of arrested sexual development.

The lesion of the testicle has, after careful study, impressed us as a congenital one. The appearance is identical with that many times described in cryptorchid testes. There is no evidence of inflammatory change, nor is the architecture of the organ disturbed by the results of old infiammatory processes. Especially significant is the preservation of the tubuli recti, which as was shown by Geoffrey St. Hilaire, develop independently, and normally form secondary connections with the testicular epithelium proper. It is hardly probable that an inflammatory process, whatsoever its nature, could produce such widespread changes in the body of the testicles, leaving the accessory conducting tubules intact.

The conclusion that may safely be deducted from the foregoing case is that the presence of interstitial cells, even in abundance, is not necessarily followed by the normal acquirement of all the secondary sexual characters.

We wish to report a second case in which the subject presented the normal masculine habitus in spite of an extreme atrophy of the testes.

Case II—Acc. No. 2,512. Male, 61 years of age.

Anatomical Diagnosis—Lobar pneumonia, suppurative pleurisy, suppurative pericarditis, infarct of lung, thrombosis of pulmonary artery, multiple angiomata of liver, fibromata and congenital cysts of kidney; hypertrophy of the prostate, atrophy of the left testis, double varicocele.

The left testicle is atrophic, measuring about 2 cm. in its longest diameter. On section, the testicular tissue is firm, showing evident increase in the fibrous tissue; the tubules cannot be pulled out with the forceps. On close inspection, there are seen

a number of slightly prominent circumscribed yellowish foci. The largest of these is about 3mm. in size. The right testicle is also atrophic, but somewhat larger than the left. Length 3½ cm. The appearance is the same as that of the other testicle. The epididymes are normal. The prostrate shows slight hypertrophy of the middle lobe and contains abundant sand. The seminal vesicles are normal.

Pieces were taken from various parts of each organ, fixed in Fleming's solution and Mullerformol, and stained with saffranin, anilin gentian violet, dilute Giemsa, and Haidenhein's iron hematoxylon.

The tubules are entirely composed of hyaline material, showing only faint indication of fibrillary structure. A distinct lumen is absent; at most, there is an irregular cleft in the central portion in which there may be found one or several degenerated epithelial cells. Between the tubules is an abundant and very cellular connective tissue. About the tubules the nuclei of the connective tissue cells have a circumferential arrangement. The interstitial cells proper form a conspicuous part of the intertubular tissue and may be readily distinguished with the low power because of their characteristic staining reaction. They are arranged either in loose strands and cell masses, or in the form of well-circumscribed islands attaining a maximum size of several mm. They are thus easily seen in the stained section with the naked eye, and doubtless correspond to the yellowish nodules described in the fresh section. Taking one of these larger islands for description we find that it is composed of a reticulated syncytial protoplasm, having almost a fibrillary structure. It is impossible to distinguish the confines of the individual cells. The nuceli are roughly oval, many of them irregular in outline. They stain rather faintly, but show a fine chromatin network, rarely a distinct nucleolus. Many of the nuclei appear shrunken and pycnotic, taking the stain diffusely. No mitoses are found. The cell protoplasm has a fibrillary character and is extensively vacuolated.

In Fleming-saffranin preparations there are present in most of the cell groups numerous black-staining globules varying in size and irregularly distributed. As a whole the fat is less than one would expect from the vacuolated appearance of the cells. The fat globules vary in the intensity with which they stain with the osmic acid, some taking a brownish tinge and others a brownish black. Fat droplets are also occasionally present within the tubules, either in the form of small, diffusely stained granules, or as larger globular masses which frequently present a foamy or vacuolated appearance; some of the globules are stained only at the periphery, leaving a lighter granular center. These incompletely stained forms are very rarely seen within the interstitial cells.

Pigment is abundantly present both in the larger cell masses and in the smaller strands of cells situated in the interstices of the tubules. It occurs for the most part as fine brownish granules, varying somewhat in size; in sections stained with dilute Giemsa the pigment takes a greenish tinge.

Blood vessels are numerous, thin-walled and congested. The larger masses of interstitial cells are especially well vascularized.

The tubuli recti are lined with a single layer of low cuboidal epithelium devoid of cilia. This epithelium shows in places distinct degenerative changes, the nuclei being irregular in shape and staining diffusely. In places the tubules are filled with a conglomorate mass of exfoliated cells.

Sections of the other testis show in the main a similar condition. There are found, however, scattered among the hyaline tubules a few groups of tubules containing well preserved epithelium showing active spermatogenesis. Especially interesting is the distribution of the interstitial cells. These are everywhere increased in number, but more especially about the atrophic tubules, between which they form thick strands, and in places, circumscribed islands. On the other hand, where the seminal epithelium is preserved, the interstitial cells, though more abundant than in the normal testis, are less noticeably increased. This observation is in direct opposition to that of Thaler, who states that the reverse is the case

The two preceding cases have been reported at length, not only because of their possible bearing upon the question as to what elements are responsible for the internal secretion of the testicle, but also because we have found no reference in the English or American literature to similar cases. The hyperplasia of the interstitial cells was so pronounced in the second case as to give rise to tumor-like nodules easily visible with the naked eye. The diagnosis in such a case is possible from the gross appearance.

In our study of the interstitial cells, we have been particularly interested in the condition of status lymphaticus, and for the following reason: The subjects of this condition present certain anatomical features which may be considered as indicating

an arrested sexual development. Perhaps it would be more accurate to speak of these individuals as failing to undergo normally and at the proper time, certain modifications of structure which in otherwise constituted persons, attend the ripening of the sexual function. Thus the typical hair distribution, as described by Norris (56), is that of immaturity, and in pronounced cases, remains so throughout life. The thymus gland, which normally undergoes rapid involutional changes at the time of puberty, persists into the third and fourth decade; the regressive changes are delayed. The average stature of these cases, as shown by Bartels (57), is above the normal—a phenomenon which is regularly observed in human and animal castrates [Tandler and Gross (55), Richon and Jeandelize (58)], and appears to be due to a persistence of the epiphyseal lines beyond the normal period [Selheim (59), Poncet (60), Lannois Pierre Roy (61) and Tandler (62)]. The average brain weight is also said to be above the normal for the age [Anton (63), Bartels (57)], and since normally the brain begins to lose weight about the time of puberty, this too may be regarded as the persistence of a juvenile condition. The hypoplastic arterial system especially the delicate and over-elastic aorta, is usually regarded as due to a defective development, but may perhaps with equal justice be ascribed to a persistence of the immature condition.

The overgrowth of the lymphatic tissue is perhaps the most characteristic feature of the lymphatic state. Whether there exist an inverse relationship between genital organs and lymphatic tissue, such as apparently does exist between testicles and thymus [Paton and Goodall (64), Noel Paton (65), Calzolari (66), Grimani (67)], remains for further investigators to prove.

From what has been said, there seems at least some basis for the belief that the perculiar anatomical features characterizing the lymphatic state—or to use Bartel's poorly chosen phrase, the hypoplastic constitution—indicate a failure on the part of the individual to undergo the customary changes of puberty. Some of these changes fall unequivocally into the category of secondary sexual characteristics—especially the growth of hair and the masculine conformation of the limbs. But indeed, all those bodily changes which customarily attend the maturation of the sexual function, may in a broad sense, be classed with the secondary sexual characters.

If then, the proper acquisition of these secondary sexual characters is directly dependent upon the internal secretion of the interstitial cells, the testis in these cases of status lymphaticus should betray some deviation from the normal histological structure. The only previous reference to the condition of the testis in cases of status is that of Kyrle (68). He found active spermatogenesis, presumably normal Sertoli cells and typical "Zwischen-zellen" in all the cases examined. As typical of the status testicle, he describes a premature thickening of the basement membrane and the supporting connective tissue. Tandler and Gross speak of "Undevelopment of the Testicle," in a single striking case of status.

Our own material included eight cases of status lymphaticus. The ages of the subjects were 7, 22 (2 cases), 24, 30 (3 cases) and 38. In two of the cases, no other cause of death could be determined.

Active spermatogenesis was found in every adult case of the series. The Sertoli cells showed no departure from the normal condition. In two cases in which the material had been fixed in Fleming's solution, the Sertoli cells contained the normal amount of fat.

As regards the number of interstitial cells, there was no difference between these cases and a large number of controls of the same ages. Thus in two of the cases, they were moderate in number, in three abundant, in three very numerous. The amount of fat and pigment likewise, did not differ from that of normal individuals. Briefly stated we were unable to find any morphological peculiarities in the testicle of the cases of status lymphaticus; nor were we able to confirm the observation of Kyrle as to the thickening of the membrana propria and the relative increase of the interstitial supporting tissue.

One of the cases included in the above series was that of an acromegalic, 38 years of age, with a very large adenoma of the anterior lobe of the hypophysis. The photograph in the original report of the case by Dr. Norris (69) shows the noticeable hypotrichosis as well as the juvenile conformation of the body. The thymus in this case was "persistent," and greatly enlarged (68 gms.). The testis proved normal in all respects; the interstitial cells if anything, were unusually abundant.*

The study of these cases, then, shows that the interstitial cells may be present or even increased in number, and yet the differentiation of the sexual characters be incomplete.

* Tandler and Gross state that they found pathological changes in the spermatic epithelium and in the Zwischenzellen in cases of acromegaly, but gave no details.

Now it is well known that influences originating outside the tests themselves may have a distinct bearing upon the sexual characters. The recently published experimental work of Crowe, Cushing and Homans (70) has shown that partial removal of the anterior lobe of the hypophysis is followed by genital atrophy in adults, or by a failure of the reproductive organs to develop, if the operation be performed on immature animals. The complete histological studies have not yet been published, but in one case (Obs. 33) separation of the stalk was followed by atrophy of the spermatic epithelium, and *increase* of the interstitial cells. Not only the spermatic function itself, but the secondary sex characters are affected by the operation of partial hypophysectomy, so that the operated animals become fat and lethargic and show no indication of sexual maturity. There are a number of clinical cases on record supporting these experimental results.

Interesting also in this connection, is the sexual precocity which has been observed in five cases of tumors of the epiphysis [(Ogle (71), Oestreich and Slawyk (72), Gutzeit (73), von Frankl-Hochwart (74), Raymond and Claude (75)], and which has led Marburg (76) to ascribe to this enigmatical organ an internal secretion exerting a special influence upon the genital sphere.

It is further well known that general paresis occurring at or immediately before the onset of puberty, is followed by a complete arrest of further sexual development. [Fairbanks (77), unpublished personal case.]

The above illustrations are cited to show that the orderly development of the primary and secondary sexual characters is controlled by complex factors—some of which at least, lie without the genital sphere itself. While it is not our intention to deny that the testicle exerts a definite chemical influence upon the whole organism, we are unwilling to admit that the evidence at hand is sufficient to connect the interstitial cells specifically with the supposed internal secretion. Not only has it been impossible to eliminate the Sertoli cells from consideration, but it has been shown that the interstitial cells may be abundantly present in cases of arrested or incomplete development of the sexual characters. It is highly probable that further research will reveal correlations and antagonisms between the genital organs and other glands of internal secretion, and that the *too* simple theory which ascribes the entire complicated series of changes attending the development of the sex characters, to the interstitial cells alone, will have to be modified or abandoned.

It is our pleaasnt duty to thank Dr. Norris, director of the laboratory, for the interest he has shown in the preparation of this paper.

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DISLOCATION OF THE ASTRAGALUS AROUND ITS ANTEROPOSTERIOR AXIS.

Operation, Reduction, Recovery, Without the Removal of the Bone.*

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All forms of dislocation of the astragalus are rare, that is, the double or total dislocation of Malgaigne, a mediotarsal and tibiotarsal dislocation, in which the astragalus has been displaced from all its articulations. There are several forms, but dislocation by rotation or version is the least often observed. Krönlein, in 400 dislocations, did not see a single case. Gray says: "This dislocation of the trochlear surface of the astragalus from the tibio-fibular mortise is not of common occurrence, as the ankle joint is a very strong and powerful articulation and great force is required to produce it."

By far the majority of cases reported have been accompanied by a dislocation of some other bone, or a fracture, either of the astragalus or an articulating fellow.

The case that is reported herewith is without a complicating fracture, or if a fracture was present it was of no consequence.

The accompanying radiographs are the first published which show the dislocation by rotation of the astragalus before and after operation.

This, together with the perfect results obtained without astragalectomy, makes the case of unusual interest and justifies description in detail.

Patient—M. Mc. N., female, 32 years of age, weight 195 pounds, in perfect health, very muscular, was admitted to my service at the Harlem Hospital, June 24, 1904.

History—While descending a flight of stairs, the patient tripped at the top and fell nearly to the bottom; she could not exactly describe how the fall commenced, but was conscious of and distinctly remembered that the initial accident at the top of the stairs was a turning in of the left foot, accompanied by severe pains in the left ankle. When near the bottom of the stairs, her left foot was caught between two uprights of the bannister and the ankle joint received, as she continued in her downward flight, a second violent wrenching, with some superficial injury to the

* Reprinted from the Journal of the American Medical Association, January 23, 1909.

overlying skin and integument. I first saw the case on the second day following the injury. Reduction by all possible means and methods, without and with anesthesia, had been unsuccessfully attempted.

General Examination—This showed the left foot somewhat inverted, sole pointing inward, slightly downward, and rather fully extended, with some elevation of the heel, which threw the skin and integument over the tendo Achilles, into two or three transverse folds or ridges, with intervening deep crevices. The external malleolus

Figure 1.—Dislocation of astragalus around its anteroposterior axis (left foot), before operation.

projected prominently, and the overlying skin was tightly stretched. The foot being so much inverted, the internal malleolus was even and smooth with the surrounding surface, and could not be seen as a usual prominence, though it could be distinctly palpated. Anteriorly, a little internal to the median line, between the malleoli, could be seen a slightly diffuse rounded projection, which on palpation could be easily recognized as the head of the astragalus, the rounded smooth surface that articulates with the navicular. By depressing the surrounding integument, the head could be firmly grasped between the thumb and forefinger, but it was absolutely immovable. Reaching from just in front of the internal malleolus, nearly to the median line, anteriorly, was a superficial sloughing skin wound, irregularly quadrangular in shape, about 1½ by 1½ inches in size. This wound was apparently produced by external violence, at the time the foot was caught between the uprights, and was not the result of pressure from within. The wound did not in any way communicate with the joint. There was almost complete loss of active motion, the foot being rather fixedly set and rigid. Passive motion, present only by force, was accompanied by great pain and rather limited. Any marked deformity of the foot was characteristically absent.

Diagnosis—A diagnosis of dislocation of the astragalus was made, but it was not definitely classed until radiographed.

Radiographic Examination—Figure 1 shows the left foot radiographed from without. inward before operation; that is, the inner surface of the foot rested on the

plate, with the foot forcibly extended, and inversion exaggerated. It will be noted that the contour of the skin, the topography of the foot, is smooth around the ankle joint. When one notes the deformity of the bony parts, he is greatly impressed by the lack of a corresponding deformity of the soft parts. This is characteristic of this form of dislocation and directly opposite to all other forms of dislocation of the astragalus An outward, inward, forward or backward dislocation will produce a marked deformity. The astragalus appears somewhat too far forward, because of the angle at which the exposure was made. If the tube had been placed posteriorly, or if the leg had been rotated a little forward, so as to bring the fibula directly overriding the tibia, in the same plane at right angle to the plate, as in Figure 2, it would then be shown, as was demonstrated by the fluoroscope, and determined at the operation, that the astragalus was situated more posteriorly, was well within and firmly gripped by the tibio-fibular mortise. The astragalus is rotated outward around its antero-posterior axis, for an angle of slightly more than 90 degrees, so that the upper surface, which articulated with the lower end of the tibia, now points outward and slightly downward. The inner surface, which articulated with the outer surface of the internal malleolus, now points upwards and articulates with the lower end of the tibia. The head of the astragalus overrides the navicular. The external surface, which articulated with the inner surface of the lower end of the fibula, now rests on top of the os calcis. The small shadow in Figure 1, between the angle of the calcaneum and the fibula posteriorly, does not admit of positive description. It was stated above that if a fracture existed it was of no consequence; if this shadow is cast by bone, it is probably only a small rim of the posterior border of the astragalus that was pulled off by the posterior calcaneo-astragaloid ligament, to which it was attached. It could not be palpated before nor during operation, and is not visible in Figure 2, and, if a fracture, was not of sufficient importance to complicate the dislocation. After a careful examination of the foot and a close study of the radiograph, Figure 1, it was apparent that the joint articulations of the astragalus were totally demolished; the ligaments, nutrient vessels and trophic nerves were surely destroyed, and it was decided that an astragalectomy was the only apparent means of saving the foot.

Operation—On July 1 the whole foot and leg were thoroughly cleansed, particular attention being given to the sloughing wound over the inner aspect of the foot. This wound was vigorously attacked, with a determination to make it sterile; it was scrubbed with soap and brush, flushed with pure peroxid of hydrogen, swabbed with pure carbolic acid, and flooded with pure alcohol; thoroughly rinsed in bichlorid, and finally run over gently with the actual cautery. All this was done because our line of incision had to be made directly through this region. The head of the astragalus was now exposed through a longitudinal incision and firmly grasped by a heavy pair of bone forceps, but could not be moved. The tendo Achillis was then incised subcutaneously; then the joint became sufficiently relaxed to allow me to withdraw the astragalus partly without the wound. It was lying so loosely within its present position that it could easily have been removed without severing a tendon or ligament or tissue of any kind, and this is what I began to do; but the ease with which the bone could be manipulated, held now by only a small pair of mouse-tooth forceps grasping the head, led me to try to replace the same; so after rotating inward it was easily reinserted in its proper position. The upper half of the wound was sutured, the lower half left open, a small drain inserted, and a wet dressing applied. This was done on account of the sloughing wound and the feeling gained from the recorded experience and teachings of others that the astragalus would yet have to be removed on account of subsequent caries. A right-angled splint was applied to the foot.

Postoperative History—There was a slight afternoon elevation of temperature for a few days following operation. The first dressing was applied on the third day after the operation. The wound was fairly clean, the eschar from cauterization, chemical and actual, separating cleanly. At the second dressing, applied on the fifth day, the wound was clean and granulating and all swelling disappearing. The drain was omitted. There was sight motion at ankle joint. From now on until July 22, the date of discharge from the hospital, recovery was uneventful. The patient walked from the hospital with the aid of a cane. On July 27, the date of the second radiograph, Figure 2, the patient was walking easily without assistance and without a limp. The wound was entirely healed; the joint was freely movable in every direction. There was no pain and recovery was complete.

The mechanism of dislocation of the astragalus by rotation is very complicated. The best explanation offered is probably that a rotating force acts on an already partially dislocated bone; whether this force is transmitted from the tibia above, or from

muscular action, or from the resulting action of two opposing forces, is still undetermined.

In the case here reported there is a clear straightforward history of two distinct injuries, the second one of which was positively that of a rotating force. The first one may have partially dislocated, or at least torn the ligaments of the astragalus.

The difficulty met by experimenters of producing the dislocation on the cadaver would suggest the necessity of live muscular action for its production.

Figure 2.—Dislocation of astragalus (left foot), after operation.

For further information concerning the mechanism of the dislocation of the astragalus, read the remarkable, if gruesome, experiments of Rochet (1).

Malgaigne reports six cases, all but one of which are rejected both by Barwell and Stimson. It appears that he reported one case twice. The case represented in Figure V, Plate XXX, of Malgaigne's "Atlas of Fractures and Dislocations," is taken from Dupuytren's "Museum." It was an old injury and showed ankylosis between the astragalus and os calcis, with rotation of about 45 degrees and some forward dislocation, Malgaigne says: "This piece has come under my hands through former information. The dislocation was rather old, as the ankle has grown (or become attached) to the heel bone. The state of the bones seems to indicate that walking may be accomplished on this foot; but the subject supports itself, only on the outer edge of the foot, while the inner edge is highly elevated, and the toes turned inwardly, as with the inverted club-foot. The picture does not show this disposition, which I have neglected, in order to better demonstrate the conditions of the ankle. Add to this that the fracture of the fibula appears to be of quite recent origin, and certainly is not of the same date as the dislocation.

"What strikes me first is the projection of the ankle head at the same time forwardly and to the outside on the cuboid and scaphoid.

"But an even more curious displacement is that of the ankle body; its pulley, turned outwardly, extends almost entirely to the inner facet of the fibula, and the inner ankle facet is found under the tibial mortise. The turning is not, however, a com-

plete quarter circle, as on the outside may still be seen a portion of the exterior ankle facet, which is hardly in contact with the peroneal malleolus pulley, and is at the same time looking downwardly and outwardly."

To Barwell (2) belongs the credit of having first accurately diagnosed, during life and before operation, a dislocation by rotation of the astragalus. Malgaigne and others had previously described this condition as impossible of diagnosis.

Barwell's very excellent report of the physical examination of a dislocated astragalus shows an extraordinary knowledge of topographical anatomy of the astragalus, recognized by palpation. Such exact knowledge is not often observed in these days, when we are learning to depend so much on the findings of the X-ray. Barwell, however, failing to reduce, did an astragalectomy. He says:

"My view is that in all cases of dislocation of the astragalus, certain and sufficient, but not too persevering, attempts at reduction should be made. If they fail, the bone, unless dislocated backward, should be at once excised. . . . When torsion is complete, the only choice lies between an utterly useless foot, excision of the astragalus and amputation."

Recent literature contains a very few reports of cases of dislocation of the astragalus of any kind, and still fewer by rotation.

C. Lepoutre (3), interne under Duret, reports a case of astragalectomy; a small pen-and-ink outline of a radiograph by Desplates is shown, in which the astragalus is rotated through less than 90 degrees.

Villar (4) reports a case of total rotation; as usual, however, he did an astragalectomy.

Croly (5) says that it is a remarkable fact that if when the astragalus was dislocated forward, forward and inward, or forward and outward, it was not removed, it acted as a foreign body; but if it went backward where it had plenty of room, it did not do any harm whatever. His strong opinion was that immediate removal of the bone with careful dressing of the wound was the proper treatment.

Stimson says:

"Expectation in irreducible compound dislocations of the astragalus has almost always ended in removal of the astragalus, or amputation, or death, and the cases will probably be very few in which primary removal of the astragalus will not give the patient the most speedy recovery, the least risk and the most useful limb.

"In compound dislocations, reduction is to be sought, unless the astragalus is entirely detached, or the lacerations are so extensive that suppuration is unavoidable Otherwise, primary removal of the astragalus or amputation is clearly indicated."

A glance at Figure 1 is sufficient to cause one to agree that this joint was totally destroyed, the vessels and nerves torn, the ligaments and articulating bursæ ruptured, and the astragalus looks not only useless, but dangerous to leave within the joint. It was the primary intention, as before mentioned, to perform as astragalectomy. When the joint was opened, however, everything looked clean and nice, and even the joint fluid was not as bloody as one would expect after a complete rupture of the interosseous ligament; and the ease with which reduction was accomplished after subcutaneous tenotomy of the tendon Achilles, together with an inherent aversion to mutilate a joint, all suggested the plan of letting the bone remain *in situ*.

The extraordinary good results in this case will invite the adoption of the same procedure in similar cases.

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INJURY AND DUPUYTREN'S CONTRACTION.*

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Dupuytren's contraction is an affection of the palmar fascia of obscure origin, characterized by slow onset and progression, leading to contractures of the fingers, and irremediable except by operation.

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It receives its name because of Dupuytren's classical description growing out of his studies and operations at the Hôtel Dieu in Paris. I have had the good fortune to receive a copy of Doane's English translation of the "Clinical Lectures on Surgery" delivered by Dupuytren, published in 1832 by "An Association of Physicians," who were apparently his students, and from this volume it appears that Dupuytren's accurate knowledge and description of the condition was originally based on a post-mortem dissection in a patient dying from an independent cause. Up to that time it was his belief, like that of his contemporaries, that the contractures depended upon tendinous or articular involvement as the fascia had not been hitherto suspected. In this connection it is interesting to note that Dupuytren's first case was that of a wine merchant on whom he operated June 12, 1811, and by making multiple minute subcutaneous incisions he was able to obtain a good result. The condition was attributed by the surgeon to the patient's occupation so frequently requiring him to lift the edges of casks and barrels, thus producing more or less constant palmar pressure. This surgeon's next case was operated upon December 15, 1811, and in this instance the patient was a coachman with a well marked bilateral affection attributed to his occupation. Mention is made of the poor general physique of the patient in explanation of the fact that only the right hand was operated upon, and that a poor result was obtained by the author's method of subcutaneous division. After operations of this type, Dupuytren insisted that a dorsal splint be worn several weeks, and his cases were apparently much benefited in many instances.

In 1834, Gayraud of Aix, as a result of dissections, in the main agreed with Dupuytren as to responsibility of the palmar fascia, but he thought that the lateral prolongations of the latter belonged to the disease and were not anatomical.

In 1864, a patient of William Adams of London, who had declined operation for his bilateral contraction of the fourth and fifth fingers, met with an accident by which ". . . the contracted fingers of the right hand were suddenly torn open, and the skin in the palm torn across . . . " There was a quadrilateral gaping wound in the palm exposing the transversely torn palmar fascia, but the tendons were intact. This surgeon excised a few torn strands of the fascia and was able to extend the previously contracted fingers, and he sutured the wound in the skin and splintered the fingers. He ends the narration of the case by stating ". . . . the healing process proceeded without interruption, and the fingers remained nearly straight without their power of flexion being lost . . . he has since died, but no recontraction had taken place . . ." This surgeon in 1879 published a small book on "Contractions of the Fingers," and in 1892 a second revised edition of the same work, the publications being based on lectures delivered at the Royal College of Surgeons. He gives credit to Stromeyer for calling attention to the subcutaneous method of treatment in 1831, but says that Delpech in 1816 first suggested subcutaneous methods, although for other purposes.

In 1875, Madelung reported as to the value of the open method of operation as performed by Busch at Bonn. Sir William Ferguson did a linear dissection of each contracted band, making a transverse incision at the constrictions. In 1876, Professor A. C. Post, of this City, did an open flap operation. In 1879 Adams published his method of multiple subcutaneous divisions with a special scalpel. In 1884, Abbe of this City read a paper at the Academy of Medicine in which he advanced a very ingenious reflex nervous theory of origin based on the following working hypothesis, which I quote in his own language:

"*First*—A slight traumatism to the palm often entirely forgotten.

"*Second*—A spinal impression produced by this peripalmar irritation.

"*Third*—A reflex influence to the part originally hurt, producing insensible hyperemia, nutritive tissue disturbances and new growth, shown in the contracting bands of fascia and occasional joint lesions resembling subacute rheumatism.

"*Fourth*—Through the tense contraction a second series of reflex symptoms, neuralgias, general systemic disturbances and a reflection of the trouble to the corresponding part of the opposite hand."

In 1886 he reaffirmed the same theory, and again in 1894 in his "Carpenter Lectures" at the N. Y. Academy of Medicine on the general subject of "The Surgery of the Hand." Under date of June 13, 1909, Dr. Abbe writes me that this original theory " . . . seems as plausible as any yet given. . . . The origin is still an unsolved puzzle. There are some cases traceable to traumatism, but not many. There are some which have marked neuroses, but most compel some research to elicit the connection between the neuralgia and the hand lesion. This remark applies to so many surgical conditions, that the absence of marked neuralgia in most, is no proof of its not being present. . . . It is more absurd to call it a rheumatic condition than a neurosis. If it be not the latter, I do not know what is the causative factor."

This hypothesis does not seem to have been given much weight, apparently, because the pathology on which it is based seems so speculative that it is difficult to conceive of a "spinal impression" registered by an almost forgotten slight trauma to the palm. Keen (who has written much on the subject), quoted in agreement by Adams, says: "Abbe's theory of a nervous origin seems to me only probable in so far as gout or rheumatism are possibly nervous in their remoter origin."

This, then, briefly is the history of this interesting ailment, and it is worthy of notice that Dupuytren's original statement as to the seat of the lesion is universally accepted, and that his method of subcutaneous incision has still applicability in a certain class of case, although his observations are now more than three-quarters of a century old.

Anatomically the palmar fascia is a fibrous apron investing the palm of the hand subcutaneously, being separated from the skin by more or less fat, and acting as a protection and serving to hollow the palm in flexion of the hand. It is divided into a *central* and *lateral* portion. This *central* main portion radiates fan-like from a narrow origin at the annular ligament; later it begins to divide on a level with the extended thumb, and there sends a fasciculus to each finger except the thumb. When each of these slips reaches the finger, it splits to pass into the lateral margins of the anterior ligament of the meta-carpo-phalangeal joint, and smaller divisions pass to the skin at the furrow where the metacarpals and digits join, and also to the periosteum of the first phalanx. The *lateral* part of the fascia is accessory and thin, and radiates to the thenar and hypothenar regions, but it does not reach beyond the level of the extended thumb. This briefly described structural arrangement predisposes to contractures on the ulnar and practically confers immunity on the radial side of the hand.

Pathologically the condition is a sclerosis of ordinary type, and it has been aptly called "Fasciitis" by Ledderhose, and the proliferation is said to take place in the arterial sheaths as well as in the individual fibrous bands. All grades of thickness are met with, and in old and well marked cases, the proliferations may be half an inch or more in thickness and almost cartilaginous in consistency. In no instance are the tendons or their sheaths involved, nor are there changes in the articulations, persiosteum or bones unless the condition is very far advanced.

The *etiology* has always been a moot point and even now no uniformly adequate cause is known to exist. From the time of Dupuytren, trauma has been held to play a part, but no one has maintained that a single or isolated injury was productive, nor is such a theory tenable. The trauma held to be causative was that incident to occupations in which the palm of the hand was more or less constantly irritated, and hence coachmen, porters, soldiers, laborers and others who did manual work were supposed to be especially liable. Dupuytren and many of his time believed repeated traumata to be the sole cause. Others hold to the view that gout and rheumatism are factors; others believed the condition to be of neurotic origin, in effect a dystrophy not unlike that seen in disorders of the central nervous system. All authors mention the fact that heredity plays a part, and that many members of a family in later years develop the condition irrespective of their occupation.

At the present time there are, then, several ascribed causes, but that trauma plays practically no part is my contention and the basis for bringing this matter to your attention. This belief hinges on the following facts:

1. *Rarity of the Condition*—There are many physicians in active practice who have never seen a case since student days, despite the fact that they number all classes of manual laborers as patients.

2. *Location of the Lesion*—The vast majority of cases affect the ulnar border of the hand which is the part least susceptible from occupations requiring grasp, push or pull manual effort. Further, the left hand is affected almost as often as the right, although the latter is most often used. Again, it usually begins first in one hand and then progresses to the other, and it is almost never symmetrical when bimanual, and bilaterality itself is against origin.

3. *Absence After Destructive Injuries*—Wounds of the palm are exceedingly frequent and often associated with infection of the tendons and their sheaths without producing contraction of the damaged intervening palmar fascia which must of necessity take part in the surrounding inflammatory reaction.

5. *Period of Onset*—The majority of the cases appear after the 50th year at a time when sclerotic processes elsewhere are in evidence and when manual labor has practically ceased.

6. *Absence in Plantar Fascia*—The sole of the foot is constantly subjected to pressure, but fascial contraction is exceedingly rare, although anatomically the plantar and palmar fascia are analagous.

7. *Occurrence in Non Laboring Class*—Cases are frequently observed in mental workers, and of 220 cases reported by Keen, 49 were in manual and 74 in non-manual laborers.

In this connection, and with the case to be presented before us, that of a motorman, it seems to me that if any occupation should predispose to this condition it would be men of this class who in their work for eight or ten hours daily fit the palm of the right hand in the rounded knob of a metal brake-handle and the left hand in the similarly shaped metal or wood controller-handle in the operation of trolley cars. I have spoken with physicians who have to do with the treatment of this class of employees and I have yet to hear of a case in which this contraction has been brought to their notice, even though some of their patients have been operating horse drawn, cable or trolley cars upwards of twenty years. So far as the steam railway men are concerned, Dr. W. B. Outten, Chief Surgeon of the Missouri Pacific Railway Company, writes me that he has personal records of over 100,000 case of injuries to railway employees, passengers and others, and he has yet to see a case arising from trauma. Inquiry among the surgeons of the local transportation companies elicits the same fact: and personally, speaking from an experience of nearly ten years in the examination of those injured in local railway accidents, employees and others, I have never seen a case in which the contraction arose from injury or occupation, and I can recall only two or three instances in which it was even alleged to have grown out of injury, and in these the claim was disputed and became the subject of litigation, proof being offered that the condition antedated the alleged accident. Likewise, inquiry among many visiting surgeons of general hospitals having to do with the treatment of the injured has brought a negative response to the inquiry as to whether they have ever known a case to arise from injury, and nearly all of these surgeons recall with difficulty ever having seen a case in hospital practice, except as a deformity of passing notice.

These foregoing facts make strong in me the opinion that injury is not a producing factor and the actual causation may yet prove to be a lesion of the central nervous system, toxic in origin perhaps. In this connection, there is on record a case in which the bilateral contractures disappeared in a well marked case after a seizure of cerebral hemorrhage. A similar remarkable case was also verbally related to me, but not in detail sufficient for recording purposes at this time.

While rheumatism and gout and occupation are frequently found in association with the disease, they appear to exist only as predisposing and not as actual producing causes, and cannot be looked upon as constant etiological factors.

The *symptoms* are slow in onset and the usual primary stage begins as a painless puckering or more or less nodulation of the skin of the palm close to its junction with the fingers, usually near the base of the ring and little finger. This may be the sole symptom, and it may and frequently does persist in that degree for five or six years, although there are some few recorded cases in which after the lapse of a shorter period some contraction of the finger begins (see Case II). When the finger becomes affected, the proximal phalanx and the one adjacent to it become involved, and the second or contracture stage is reached. This may affect one finger alone, or may invade the adjacent digit; the usual order is for the ring finger to show the initial and most marked change, with or without involvement of the adjacent little finger. In 263 cases cited by W. W. Keen and Nicholls, the ring finger was affected in 249; the little finger, in 194; the middle finger, in 93; the forefinger, in 24; the thumb, in 12. The same author says that in 223 cases the right hand alone was affected in 70, the left in 35, and both in 125 instances. Hoffa reports 1.59% of this contraction in 1,444 cases of deformities; in 227 cases there were 180 men and 40 women. In 198 recorded cases, heredity was a factor in 25.2% of patients. It is exceedingly rare in children; however, one case at 6 months and a few congenital cases are narrated.

In another class of case, contraction of the finger at the metacarpo-phalangeal junction is the initial sign, the nodulation and puckering rugae in the palm occurring as later manifestations. After the process has gone on in one hand to a moderate or greater degree, the opposite hand often becomes affected, usually to a lesser extent, but generally with involvement of corresponding portions. A well marked case will show, then, contraction of one or more fingers (generally the fourth and fifth), with visible raised, tense, hard fascial bands reaching from the palm to the metacarpo-phalangeal joint like violin strings, with often transverse rugae and nodules. In a severe case the fingers will be contracted sufficiently for the distal phalanx to touch the palm, the latter being irregular from numerous nodulations and rigid fascial strands. The distal phalanx can usually be extended, but the proximal and central phalanges are firmly fixed in flexion, but can be further flexed by relaxing the binding fascia, this being a differentiating sign.

From the beginning of the initial nodulation or contraction to well marked deformity, many years will usually elapse; and in certain cases two decades intervene before the contractures reach extreme grade, although all cases tend to get worse even after an apparently stationary period. There are a few cases seemingly acute in type, but the history in these is generally unreliable as to the actual initial symptoms because nodulation may exist a long time without comment, or be attributed to other causes. (See Case II.)

Treatment is unavailing by apparatus designed to forcibly correct the deformity, and operation is the only method affording more or less complete relief.

Two operative procedures are in vogue, namely: subcutaneous incisions and open dissection by longitudinal excision or by flaps. The method of multiple incision by a special tenotomy knife is that practiced mainly by Adams of London, who, as already stated, has had good success with this method, and he has many followers. He makes on the average six small longitudinal incisions at the sites of maximal contractures, and then transversely severs the binding fascia as completely as possible

Nodulation and Puckering.

by successive nicks from above down, meanwhile extending the digit as he incises. In extreme cases he has made as many as twenty-three incisions, each designed to liberate a series of contracting fibres. He immediately applies a splint which is constantly worn until the wounds have firmly healed, and it is then gradually dispensed with. He first advocated this method in 1879; and writing in 1892, he employed the same technique with modification only in so far as he now advises immediate extension rather than seeking same gradually by splints after operation.

The flap method of Kocher, and others, dissects a triangular or quadrilateral section of skin from the palmar fascia and then excises the latter; or, following the method advocated by Keen, the initial incision includes the palmar fascia in the skin flap and then dissects the fascia free from the skin by an incision that runs along the ulnar border from the inner part of the hypothenar eminence to the web between the ring and little fingers, thence transversely to the web between the index and middle fingers, and thence upward to about the middle of the thenar eminence, this making a "U" shaped flap, with the base well above the middle of the palm. After all the prolongations are released, the fascia is dissected from the underlying skin, and the latter is sutured in place.

The flap method is the one of choice especially in advanced cases, the disadvantage being that when the deformity is corrected there often remains a gap at the lower portion to be later filled by granulations; also because the lateral accessories of the fascia to the metacarpal and phalangeal regions are often hard to reach, and it is frequently impossible to divide them sufficiently to permit perfect extension and not infrequently sloughing of the flap ensues. The operative relief is usually prompt, although it may be incomplete, and there does not appear to be much chance of recurrence if the after treatment succeeds in keeping the fingers in their restored position, and if there is no secondary contraction of newly formed granulations. Splints (dorsal or palmar, or both) are worn for about two weeks, and then massage and passive motion are begun, soon to be succeeded by active motion designed to favor extension. In selected cases local anasethesia can be used by infiltration of the palm; and in some cases, exposure of the median and ulnar nerves has been made and the dissection proceeded with after these nerves have been infiltrated by cocain or allied agents.

The differential diagnosis is easy, as the main, clinically allied conditions are those of so-called "hammer finger" or "trigger finger" and contractions of congenital, cicatricial and tendinous origin. Each is readily excluded by the history and the

Contraction IV and V Finger and Nodulation.

distribution of the contraction and the absence of nodulations or superficial longitudinal palmar bands, and by the ability to overcome in some degree the existing deformity by manipulation.

In the absence of nodulations and longitudinal visible or palpable bands radiating from the palm, a diagnosis of typical Dupuytren's contraction should not be made, especially if the proximal and central phalanges can be extended.

The following case is presented by the courtesy of Professor John F. Erdmann:

Case I.—John J., 54 years of age, Irish, married, motorman.

Family History—No bearing except that his mother was rheumatic. No contractures or deformities in family.

Past History—Negative except that he has been markedly rheumatic. A heavy drinker. Has been a motorman about 9 years; prior to that did various kinds of manual work.

Present History—Twelve years ago he noted a dimpling at base of *left* little finger, soon followed by contracture of that digit. Later the adjacent fingers became involved, and soon all were affected except thumb. Two years after the onset in left

hand, the *right* hand became involved, but to a lesser degree. In April, 1907, left hand operated upon by Dr. Erdmann at Gouverneur Hospital, and in April, 1909, he appeared at Dr. Erdmann's Clinic for operation on the right hand.

Examination showed palmar fascia contraction of right hand, the inner four fingers being strongly flexed, the ring and little finger most markedly, but despite this he was able to do his work and operate a trolley car. The left hand showed an operative palmar scar with some contraction of the little finger, but good function of the hand; patient states that before operation the finger tips almost touched palm.

Operation April 12, 1909, by Dr. Erdmann. Triangular flap method with exsection of the very dense fascial strands and gradual extension of involved digits. Lateral prolongations difficult to release, especially on ring and little finger.

Post-operative History—Healing per primam except at base of flap which later healed by granulation. Splintage for about two weeks, and thereafter gradually increased passive and active motion. At this date, wound firmly healed and dressings have long ago been discarded. Function and normal appearance restored to a marked extent.

Dissection Contracted V Finger.

The following case was seen by the writer at Harlem Hospital, in June, 1909:

Case II—William S., 58 years of age, English, single, cook.

Family History—Of note only in so far as his father died of rheumatism and his mother of cancer. No family deformities.

Past History—Always a heavy drinker. Has had "rheumatic twinges" in various joints at irregular periods for years. In English army for 12 years. Has done all kinds of manual work.

Present History—Four months ago noticed a "lump" at base of *left* little finger, and this was almost immediately followed by contraction of that digit at palm; soon the adjacent three fingers similarly involved, but to a lesser extent. One month ago, same manifestations began in *right* hand.

Examination showed bilateral contraction of palmar fascia, more marked on left side where little and ring finger are folded so that their tips are within an inch of palm. Four inner left fingers affected; little and ring finger on right side only involved. Nodosities and rugae well marked.

Operation June 21, 1909, by writer at Harlem Hospital. Quadrilateral flap on left palm with palmar fascia included and later dissected free from skin (method of Keen). This is difficult, and I would not do it again in the same class of case. Lateral prolongations at ring and little finger hard to release.

Post-operative History—Part of base of flap sloughed from deficient blood supply, probably due to undue removal of underlying fascia or tension. Granulations filled

Case II, before Operation.

in the gap and fingers remained straight except for some flexion of little finger; final result cannot be narrated, but it promises to be good.

Later: Opposite hand relieved by multiple subcutaneous incisions after method of Adams. Both hands much improved.

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A MODIFIED OPERATION FOR INGUINAL HERNIA.*

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An apology is perhaps expected from any one who would venture to suggest a new operation for the repair of inguinal hernia when the many already at our command seem to meet all the essential requirements. But the offense is perhaps miti-

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gated when it is proposed to deviate from the usual procedures only in one particular step, with the single object in view of simplifying the operation as a whole. Any suggestion in technic which obviates undue manipulation of tissues has much to commend it and should be accepted, provided the basic principles of the operation are complied with and adhered to. The success of any operation for hernia depends, in no small measure, among other things, upon the least possible trauma to tissues and structures, which result is not always incident to the usual methods of ablation of the sac. The prevailing technic of isolation of the sac and the transplantation of the

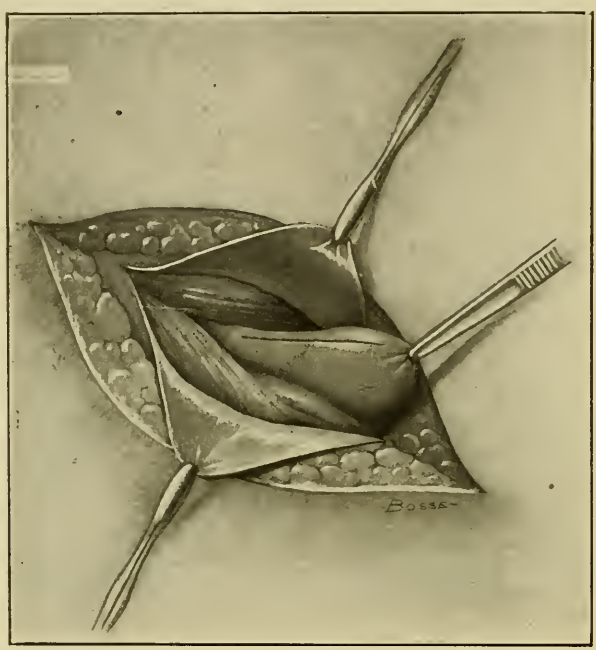

Figure 1.—Skin of superficial fascia and external oblique have been incised, showing bulging hernial sac. Incision through sac is indicated.

cord has no good anatomical, physiological, surgical, or mechanical advantage, and should therefore be characterized as an unnecessary refinement. Upon this basis the proposition advocated in this paper is suggested and advanced as entirely compatible with safety and efficiency, combining, as it does, all the essential requirements and principles.

The feature of the operation now under discussion lies in the treatment of the hernial sac which is permitted to remain in its bed practically undisturbed. In other details, it follows the procedures usually employed and generally accepted.

The principles which underlie the rationale of the operation and form the basis of the technic may now be briefly considered. In the normal descent of the testicle, a diverticulum of peritoneum, the processus vaginalis, precedes it clothed with its mesorchium, to its final resting place in the scrotum. At a certain stage, therefore, there is a communication between the processus vaginalis and the abdominal peritoneum. Later this communication is lost by an obliteration of the upper part of the diverticulum, so that the testicle lies in its scrotal bed covered by a serous layer derived from the abdominal peritoneum, but having no connection with it. A similar process of obliteration and blending of the peritoneum is observed in the peritoneal development of the pancreas. When first developed this viscus possesses a complete peritoneal covering, lying between the two layers of the posterior mesogastrium. At this stage, then, the stomach has changed its position by rotation, carrying the pancreas with it, the now posterior covering of the head of the pancreas lies in contact with the serous covering of the right kidney and soon becomes obliterated by absorption. In like manner the stomach by its further adaptation to the cavity of the abdomen carries the tail of the pancreas to the left, causing its posterior layer of

peritoneum to lie in contact with the left kidney and its peritoneal covering. The same process of obliteration takes place and the pancreas now lies wholly in the retro-peritoneal space. A further review of other viscera as regards the development of their peritoneal relations need not at this time be considered, since the formative processes exhibited by the pancreas serve sufficiently to illustrate the fact that contiguous layers of peritoneum brought into contact adhere, blend and obliterate. That the adult peritoneum is capable of such blending and obliteration is well illustrated in intestinal anastomosis in plication of the gastro-hepatic omentum and stomach, and in all conditions where peritoneal suture is employed. Whatever be the methods of securing peritoneal apposition, or whatever be the conditions for its employment, the histological findings reveal that the resulting union is continuous and that the peritoneum as such has lost its identity. Matas in his article on the "Radical Cure of Aneurism," *Annals of Surgery,* February, 1903, regards the aneurismal sac as a large diverticulum or prolongation of the parent artery with which it is connected. Quoting further from this paper, he observes that "the lining membrane of the sac is a continuation or expansion of the endothelial intima which lines the interior of the artery, and in fact of the entire vascular system, and that the sac itself, when not disturbed from its vascular connections, is capable of exhibiting all the reparative and regenerative reactions which characterize the endothelial surfaces in general when subjected to irritation." The analogy between the aneurismal sac and the hernial sac is apparent. And it is also clearly evident that the hernial sac is a prolongation of the abdominal peritoneum and as such will exhibit all the tendencies to occlusion and obliteration, when carefully approximated by suture. And, further, it may be added

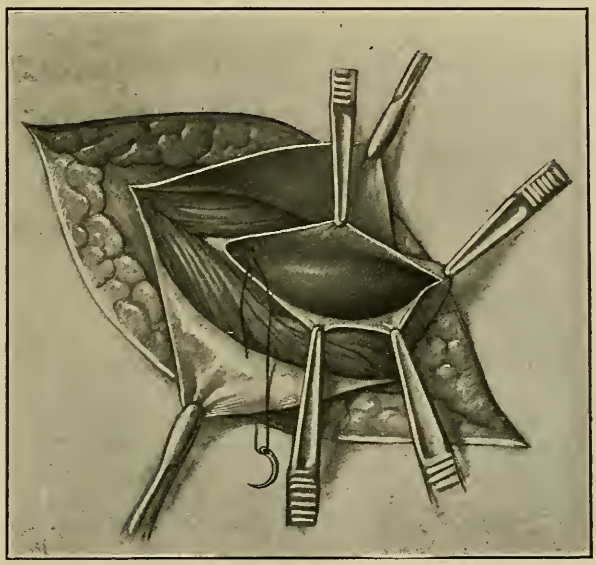

Figure 2.—The purse string suture has been placed well within the lumen of the sac. Traction on the sac will insure the placing of the suture sufficiently high to avoid any pouching at the site of the internal ring.

that whatever be the gross change in the hernial sac, its peculiar identity remains, and its interior when subjected to pressure and irritation is still capable of a reaction as described above.

These brief preliminary remarks serve to introduce the details of the operation, which are as follows:

The skin and superficial fasia are incised, exposing the bulging sac and its intimate coverings. The sac is further exposed by incising the external oblique aponeurosis, in a direction parallel to its fibres. The sac is now revealed (Fig. 1) and in accordance with the proposed modification, its relations to other structures of the canal are left undisturbed and no dissection whatever is attempted. An incision is made in the longitudinal axis of the sac (Fig. 1) its contents thus being exposed, are inspected and returned to the abdominal cavity. The interior of the sac is now

rubbed with a gauze sponge or scarified with the point of a needle, so as to more readily favor the cohesion of its subsequently opposed peritoneal surfaces. The next step is the closure of the sac at the internal ring. With a well curved needle carrying plain catgut No. 2, a purse string suture is placed well within the lumen of the sac, as illustrated in Fig. 2. A little traction on the sac will insure the placing of the suture sufficiently high and will thus avoid any outward bulging of the peritoneum at

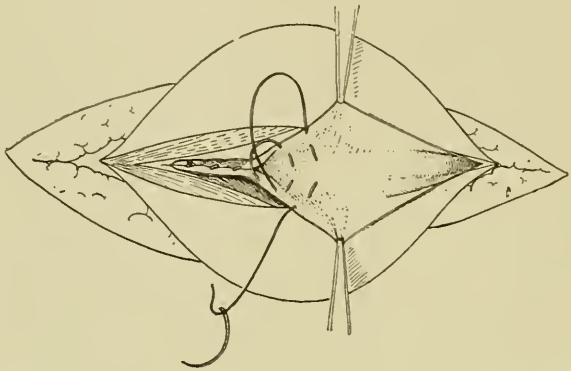

Figure 3.—Schematic Line Drawing Showing Obliteration of the Sac With Continuous Suture. In the Illustration the Sac Has Been Much Elongated in Order to Show the Method of Suture Better. Five to Eight Sutures Will Ordinarily Suffice to Effect Closure.

this situation. The suture penetrates only the peritoneum, and the needle is guided in the avoidance of other structures of the canal and cord by the same principles which obtain in peritoneal technic in general. The inclusion of any part of the cord, therefore, in this or in the following step of the operation is a remote contingency. The portion of the sac distal to the purse string suture is now obliterated by a continuous suture as depicted in the diagrammatic line drawing (Fig. 3). The final step in the obliteration of the sac is the placing of a running suture which approximates the sac and its intimate coverings at the site of the incision which revealed its interior. After disposal of the sac as described, the formation of a new anterior wall is effected in the usual manner, by suture, with interrupted kangaroo tendon, of the internal oblique and conjoined tendon to the sharp shelving border of Poupart's ligament. The cord and its structures, however, are permitted to repose beneath this new anterior wall, and necessarily so, since there has been no dissection of these structures. This burying of the cord is similar to the method advanced by Ferguson and now generally adopted as an advance over the former procedure of transplantation as in the Basini operation. In the final steps the aponeurosis of the external oblique is sutured with plain catgut No. 2, and the skin with fine gut or silk. A résumé of the foregoing shows but a single deviation (suture obliteration of the sac) from the steps of the usual operations, which in their sac dissection necessarily inflict varying degrees of trauma on the sac itself, the cord and testicle, and make uncertain the integrity of the nerve supply. In the author's modification it is to be noted that the cord or testicle are, at no time during the operation, disturbed or manipulated.

The essential principles underlying the operation for inguinal hernia may be embodied under two heads: closure of the sac at the internal ring, and the formation of a new anterior wall for the inguinal canal. In other words, the aim of the operation is to restore the rotundity of the peritoneum and to construct a barrier which shall act as a restraining wall against the protrusion of any viscus through the internal ring. All operations have these points in common and they differ only in the way in which they are effected. A consideration of the second of these aims is foreign to our present discussion and deserves no criticism. A choice of operation then depends upon which method appeals as being least involved and easiest of accomplishment. The prevailing technic of effecting the first of these steps the writer considers superfluous at the cost of inviting unfavorable complications, both immediate and remote. And even in the absence of complications, this detail we consider without manifest advantage. That the same closure at the internal ring may be attained by a simpler technic consuming less time is very apparent in view of our previous obser-

vation, that when endothelial surfaces have been approximated and have been subjected to irritation and constant pressure, the inevitable result is one of obliteration, based on the embryological and histological data considered in our introductory remarks.

Even though the author's claim of a time-saving factor should not enter in the consideration of this modification, the advantage would still be in favor of suture obliteration, if for no other reason than that which is inherent in a non manipulation of the cord and other structures at the canal. Moreover, I am certain that suture obliteration may be accomplished in considerably less time than is required for isolation and resection. This fact has been repeatedly shown but it is scarcely justifiable to suggest this element as the prime argument in favor of this newer procedure. In the smaller herniae the modification cannot serve to an advantage as far as the time element is concerned, since isolation in these cases has always been a most easy and rapidly performed step. In the smaller herniae, then, we may dismiss a consideration of the rapidity and emphasize the other advantages. In the larger herniae with thick and densely adherent walls, however, rapidity does enter as a striking factor, and it is in these cases that all the advantages claimed for the modification obtain in full significance.

The possible criticism which is likely to arise in connection with suture obliteration of the sac has not been left unconsidered in my clinical observations. A natural

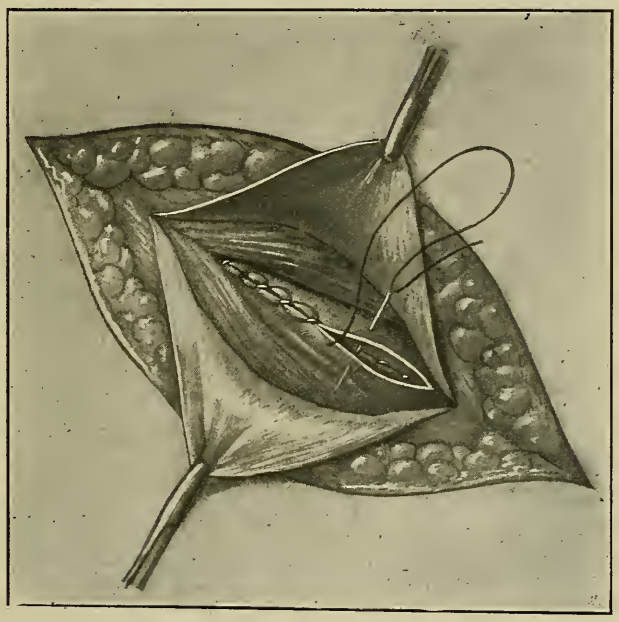

Figure 4.—Shows the Continuous Suture in the Final Step of Complete Obliteration. Figure 5 Shows the Same Suture, But in a More Diagrammatic Way. The Sac is Seen to Blend With Its Adjacent Structures and Its Margins Therefore Have Not Been Outlined as in the Following Schematic Illustration.

doubt arose in my earlier cases as to the behavior of the remnant of the sac so left. It is sufficient to say that no pathological condition of the distal portion of the hernial sac has been observed, or has occurred, which fact is in harmony with the principles already set forth. The formation of a cyst or hydrocele is most remote and quite impossible if the inner surfaces of the sac have been accurately and carefully approximated. Aside from the pressure and irritation applied from within the sac we must concede the presence of a positive pressure effected by the overlying structures, as a significant factor in the process of effacement. In the McEwen operation, the sac, though isolated, is not cut away, but is applied as a pad at the site of the internal ring. Even though deprived of its vascular supply, autopsy report shows this pad of peritoneum completely absorbed. (*Von Bergman's System of Surgery.*)

In conclusion we would submit that the dissection of the sac has no anatomical

or surgical advantage, and should therefore not be insisted upon as an essential requirement in the details of the operation. If the continuity of the peritoneum at the site of the internal ring has been restored, and the portion of the sac distal to this, obliterated, the first principle in the radical cure of hernia has been attained.

It is only fair to say that the uniformly good results which have attended the cases up to the present have been an encouragement to further trial, with the firm

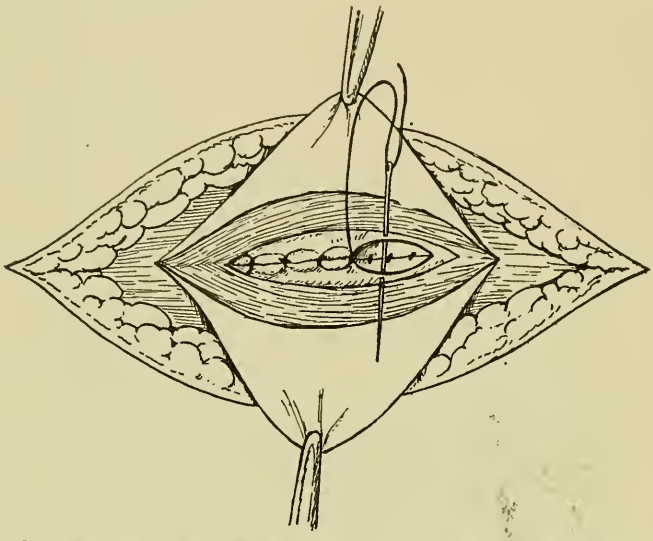

Figure 5.—Schematic Drawing Showing Final Suture as in Figure 4, But More Diagrammatic. This Suture, as Will be Noted, Approximates That Portion of the Sac Which Has Not Been Included and Opposed by the First Suture. This Suture May be Omitted if the First Has Been Introduced Sufficiently Near the Edge of the Sac Wall to Insure an Apposition of Its Entire Endothelial Surface.

conviction that subsequent experience will fully justify our present attitude. An experience with some twenty odd cases without a single untoward circumstance, I believe, warrants this preliminary presentation.

The advantages of this simplified technic may be summarized under the following heads.

1. Rapidity of performance.
2. Diminished period of narcosis.
3. No dissection of sac, and tissue bruising therefore eliminated.
4. Preservation of nerve distribution.
5. Absence of the sometime troublesome venous hemorrhage.
6. No manipulation of the cord, its vessels or the testicle.

We may further epitomize the above headings in the one word *simplicity,* which in the broadest sense, combined with efficiency, implies ideal surgical technic.

SOLITARY PERFORATION OF THE ILEUM ("PROXIMAL ULCERATION OF INTESTINAL OBSTRUCTION") ASSOCIATED WITH STRANGULATED AND OBSTRUCTED HERNIAE, REPORT OF TWO CASES WITH RECOVERY.*

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Under the name of "Dehnungs-geschwür" (distension ulcer), Kocher has described a condition of solitary perforation or ulceration of the intestine in connection with the various forms of intestinal obstruction. He believes that the importance of

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these lesions has not been sufficiently recognized and it would seem that his contention is well founded since the text-books, with few exceptions, fail to touch upon the subject,

Of the following two cases the first was operated upon in December, 1908, in the service of Dr. Rogers; and the second in the service of Dr. Erdmann, in August, 1909, both at Gouverneur Hospital.

To Doctors Rogers and Erdmann the author desires to express his appreciation for the privilege of operating.

Case I—Previous history negative as to alcohol and venereal diseases. She has had several children and the youngest is sixteen years of age. Has always suffered from constipation. She gives a history of a left-sided inguinal hernia of many years standing; has worn a truss which has always been ill-fitting. Present history dates from the afternoon of the day of admission, when the hernia became suddenly irreducible and very painful. It was several hours before her physician could be reached and upon his arrival he found that the patient herself had reduced the mass. She relates that before the replacement of the hernia, she was seized with violent pain in the abdomen, most severe in the region of the umbilicus. Subsquently she vomited several times and with the increasing pain, became prostrated. The tentative diagnosis of reduction *en bloc* was made by her physician. On admission to the hospital her temperature was 101.6°, pulse 88, respirations 24. Examination of the abdomen showed considerable distension. There were present marked rigidity and tenderness; the latter was more pronounced about the umbilicus. The liver and spleen were not palpable. Taking into consideration the previous history, the diagnosis was rather uncertain.

An exploratory incision was made just below the umbilicus. Upon incising the peritoneum a moderate amount of sero-purulent fluid and some feces were revealed. The intestines were covered with fibrin flakes of beginning peritonitis. In the lower part of the ileum there was found a round, solitary perforation with well defined edges and about one-half inch in diameter. This was closed with a pursestring suture of Pagenstecher thread and reinforced by several Lambert sutures of the same material. The intestine and mesentery about the perforation were entirely normal. However, about eight to ten inches distal to the perforation, the gut was found markedly contused, showing signs of recent strangulation. There was no solution of continuity of the peritoneal layer and the intestine responded to the usual tests for viability. It was therefore returned. The peritoneal cavity was sponged out and the abdominal wound was closed by tier suture leaving a small aperture for a cigarette drain. Owing to the patient's condition the hernia was not repaired. For three days following, the patient vomited at frequent intervals small quantities of greenish fluid; her tongue during this time was heavily coated and leathery. From the cessation of these symptoms the recovery was rapid and without incident. Blood specimens were Widal negative.

Case II—Italian, 50 years of age. He is a moderate drinker of beer and whiskey. About eleven years ago he sustained an injury to his left eye which was later enucleated. Six years ago he received a fracture of the left leg. He gives no history of gastric or intestinal disturbances. He has had a right inguinal hernia for two years and has worn a truss. On the afternoon of the day of admission his hernia came down into the scrotum; soon thereafter it became painful and tender and later he was seized with colicky pains in the abdomen; there was no vomiting. His bowels had for several days been constipated. His abdominal pain increased in severity and late in the night he was removed to the hospital. His chief complaint on admission was pain in the abdomen. Of his inguinal tumor he complained but comparatively little. Examination of the abdomen showed moderate distension. There was marked general rigidity and maximum of tenderness about the umbilicus. There were no masses palpable. Examination of the right scrotal region disclosed a large painful mass which with manipulation became reduced. The blood count showed a leucocytosis of 12,000 with 86% polynuclears. The temperature was 102.8°, pulse 100 and respiration 36. Before being taken to the operating room the patient vomited a dark greenish fluid.

Under anesthesia an incision was made in the median line. Upon opening the peritoneum there escaped a quantity of dark brown fluid, and upon separation of the presenting coils of intestine there appeared a small stream of feces leading from a perforation. This was identical in appearance with the one described in the first case—round, with well defined edges, and about half an inch in diameter. About the perforation there was no alteration in the bowel wall and neither was there any induration. An examination of the gut distal to the lesion disclosed no gross alteration as described in the first case, indicating that the degree of compression had been of

less severity. The perforation was closed with suture of Pagenstecher, and the peritoneal cavity cleansed as far as possible with saline sponges. The abdominal wall was sewed up in layers and two cigarette drains were introduced. The hernia was not repaired. The day following the operation the temperature was normal, but on the seventh day had risen to 100°. The pulse during this time remained about 100. At the end of two weeks, during which time the temperature had risen occasionally to 102°, there was no further elevation. During this period the patient complained of colicky abdominal pain and was constipated, so that daily enemas were necessary. At the end of three weeks the abdominal wound had healed and the bowels moved without aid. Widal reaction, negative.

There are several points of interest in the history of these cases. In the first case the onset of the strangulation was quite sudden and acute, and the damage inflicted upon the intestine was considerable, as revealed by the abdominal operation. It is interesting to note that the mass was reduced by the patient herself.

In the second case the hernia likewise suddenly became irreducible, but with less severe symptoms. The pain in the scrotal tumor was but slight and was entirely overshadowed by that in the abdomen. The ease of the reduction was surprising and was unlooked for. It had remained unreduced for nearly ten hours. This case points to the fact that comparatively slight damage to the intestine may be followed by such a lesion as described. Both patients presented themselves with histories and symptoms which would admit of no diagnosis except as revealed by exploratory laparotomy. Having in mind the condition as found in the first case its presence was conjectured in the second.

For an explanation of this interesting lesion we must turn to Kocher, who states that the common cause of death in all forms of obstruction by strangulation as well as by stricture, whether acute or chronic, is not due to such strangulation with local gangrene and ulceration, but by lesions in the intestinal wall above the seat of obstruction. These lesions consist in the formation of circumscribed necrosis of the mucous membrane, going on to sharply circumscribed ulceration through the whole thickness of the wall, giving rise eventually to perforation. The cause of these ulcerations is not, as has been described, due to the presence of hard fecal masses pressing for some time on the same spot; neither is it due to any lesion of the mesenteric vessels. The same lesion of ulceration is found in the ileum and jejunum where the bowel for the most part is filled with liquid contents. Kocher has experimentally distended the bowel with gas and fluid and has produced the same lesions. By such distension and without the slightest interference with the mesenterial circulation, the bowel becomes quite blue by reason of venous stasis. As a consequence of this, ecchymosis may form in the mucous membrane, the nutrition is altered and the protective influence of the epithelium (Cassin and Charrin), which has been proved to be of such importance, is destroyed. Under the influence of the increasing venous stasis and of the absorption of the increasing toxic products, there results a necrosis of the mucous membrane (beginning at the above-mentioned ecchymotic spots) going on to ulceration and perforation.

Under the title "Follicular Perforation of the Ileum," Brewer, in 1899, presented before the New York Surgical Society, a specimen obtained from a woman forty years of age, suffering from a strangulated femoral hernia which had existed four days. An immediate operation was done. About seven inches of very dark intestine were found in the hernial sac, which also contained a certain amount of dark colored fluid. As soon as the constriction was relieved, the color of the gut improved and it was decided to drop it back. After twenty-four hours the patient developed symptoms of peritonitis and died very suddenly. At autopsy, as soon as the abdomen was opened free gas and pus escaped through the incision, showing that a perforation existed. The portion of the gut which had been strangulated, although somewhat necrotic in parts, showed no perforation; but seven inches above the strangulated area there was found a distinct perforation of the ileum; the peritoneal surface was the seat of recent adhesions and the mucous membrane in the neighborhood was in a state of acute enteritis.

A fairly diligent search of the literature reveals but scant reference to this condition, which at once must be recognized as a most important complication of ileus. Erdmann has referred to it in his article on "Strangulated Hernia" (*N. Y. Medical Journal*, March 12, 1904). The contribution on "Intestinal Obstruction" in Vol. IV. of Keen's Surgery, describes the morbid anatomy of the lesion. Kocher's contribution "Ueber Ileus" is to be found in *Mitteilungen aus der Grenzgebeiten der Medizin und Chirurgie*, 1898-1899, Volume IV. Van Zwalenberg has referred to Kocher's work in the *Annals of Surgery*, November, 1907. Reports of operated cases I have been unable to find.

The term "Distension Ulcer" is apt to convey the impression that a considerable amount of pressure and distension are necessary in the production of the lesion. In my cases the distension of the pre-ulcerous stage was not marked—least in the second case (obstruction by obturation), and it is believed that the fermentative processes under bacterial influences are the most important factors. The actual perforation in my cases took place rapidly and prior to the possible formation of any considerable distension and I would therefore, while not denying this as one of the necessary and constant conditions in the production of the lesion, attach a lesser degree of importance to "distension" *per se* than is implied in the term "distension ulcer." A "distension ulcer," for example, might easily be understood to be a result of a distended intestine's inability to withstand an inward pressure, when in reality the lesion is a more complicated process. It is the result of more than a bursting or *over* distension. This term most likely arose from the fact that in animal experimentation distension was the most striking accompanying condition. But it is clear that it is impossible to produce experimentally the exact conditions present in clinical cases. With a view of obviating that which is misleading in the older term from a clinical point of view, I would suggest the term "Proximal Ulceration of Intestinal Obstruction" when referring to these lesions. Such a designation is sufficiently comprehensive and in the suggestion I merely associate the lesion as a complication instead of attempting to make it descriptive and incorporating one etiological factor, as in the hyphenated term of Kocher. "Proximal Ulceration" would still be a fitting designation whatever be the finally accepted views as to the etiology.

In conclusion, I would emphasize the single point of the importance, in our cases of hernia with acute symptoms, of making careful inspection of the intestine above the site of compression or strangulation. Reports of clinical cases will add to our knowledge of the subject.

PERMANENT COLOSTOMY.*

An Improved Original Operative Method.

Howard Lilienthal, M.D.

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The formation of an artificial anus for the permanent relief of obstruction of the lower bowel is regarded by most surgeons as a loathsome makeshift for the prolongation of life. The mental picture of such an opening suggests the constant uncontrollable discharge of fæces and flatus, the painful and annoying dermatitis in the neighborhood of the exposed mucosa and the necessity for constant change of dressings—in short, a condition of actual and permanent disability for the ordinary duties and pleasures of life. Various forms of apparatus—valves, obturators, etc., have been devised for holding the discharges in check, all more or less uncomfortable to the patient and all inefficient in action.

For at least eight years I have been performing an operation which obviates nearly all the discomfort and filthiness of colostomy. The patients have absolute control of the bowels and can even hold a considerable quantity of fluid injected into the colon. The bowels move once or twice a day, the patient knows when the movements are about to occur and—not by any means the least advantage—he is not annoyed by the necessity for wearing an appliance for obturation. The operation has been tested many times and the patients have been for the most part carefully followed up. A description of the steps of the operation follow:

An incision about 3½ inches long, more or less, is made over the outer third of the left rectus muscle and parallel with its fibres. The upper end of this incision is just about on a line between the umbilicus and the left anterior superior iliac spine, but the exact length and location of the wound depends somewhat on the amount of subcutaneous fat present. Through this incision the fingers explore the abdominal organs and the type and limitations of the stricture or tumor are learned.

* Read before the Section on Surgery of the New York Academy of Medicine, April 1, 1910. Reprinted from Annals of Surgery, September, 1910.

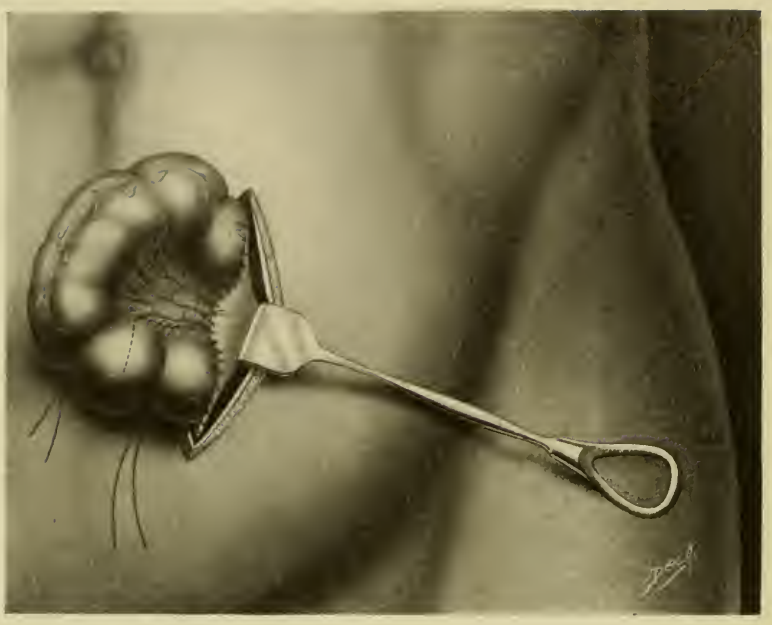

Fig. 1.—The dotted line shows line of section. The blunt retractor holds outer third of rectus muscle together with skin and aponeurosis.

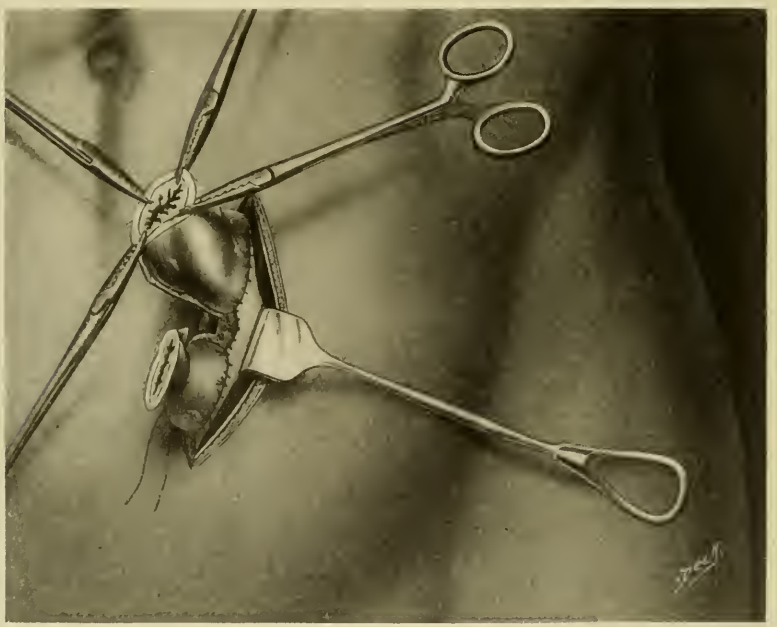

Fig. 2.—Redundant bowel and mesocolon cut away. Twisting of the intestine begun.

Fig. 3.—Twist complete and maintained in position by anchor sutures holding sigmoid to aponeurosis.

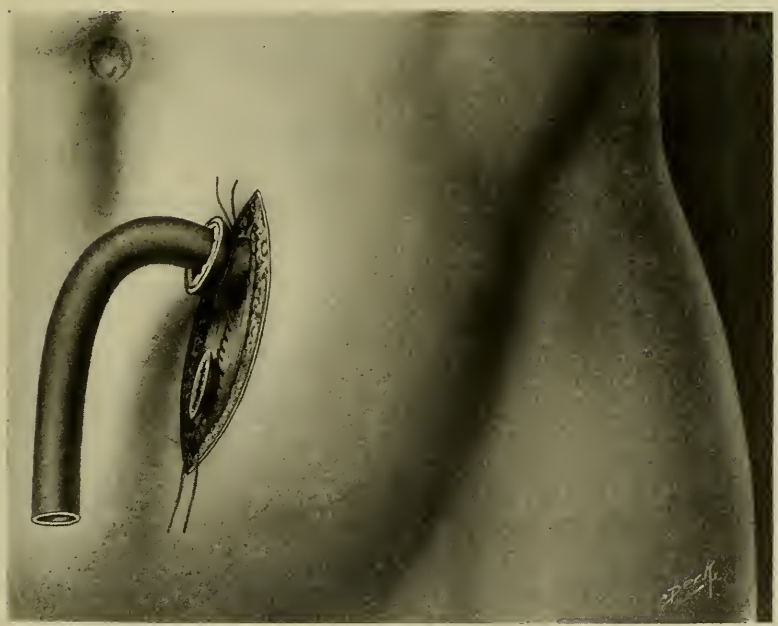

Fig. 4.—Operation complete. Aponeurosis further stitched to intestine and wound closed, with the exception of the skin.

The sigmoid flexure, be it well developed or not, is drawn out. As is well known, this part of the intestine varies greatly in length, but all is taken out which can be withdrawn without tension. The two legs of the loop are separated as widely as possible, the upper leg being sutured to the peritoneum and posterior rectus sheath in the upper angle of the wound, and the lower is sutured in a similar manner to the inferior angle. Silk or linen thread is the suture material, and the stitching is done by the continuous method, every third stitch being tied so as to avoid purse-stringing. The mesosigmoid is now sutured through and through to the peritoneum on each side (Fig. 1).

At the lower leg of the loop the gut is doubly ligated very tightly with heavy silk or cotton twine. Section is carefully made between the ligatures, taking care to avoid soiling from the small amount of imprisoned intestinal contents. Pure carbolic acid on a gauze sponge is used to sterilize the mucosa. Chain ligatures of catgut or silk are now passed through the mesosigmoid so as to prevent hemorrhage, and this membrane is then cut across. We now have a short piece of sigmoid, the distal leg of the loop in the lower angle of the wound and a long piece sutured in the upper angle of the wound. The remainder of the mesosigmoid is cut away from the long piece of intestine, freeing it completely. The entire wound is now protected by gauze packings, the peritoneum by our previous procedures being entirely closed off by suture. We should have about 3 or 4 inches of free sigmoid at the upper angle of the wound. If there is more it should be ablated. Four equidistant clamps are now placed at the edge of this upper piece of intestine, the gloved finger is inserted into the lumen of the gut to the place where it is held to the peritoneum by suture; an assistant rotates the clamps so as to twist the gut around its longitudinal axis, after the manner described by Gersuny, from 180 to 360 degrees according to the texture and thickness of the walls of the sigmoid with which we are working. By withdrawing and reinserting the finger from time to time the degree of constriction which this manœuvre produces may be accurately gauged. When this seems to be sufficient for the purpose—a matter of individual judgment—a few interrupted silk or linen sutures passed through the visceral peritoneum and submuscosa to the aponeurosis of the external oblique, hold the rotated gut in position. It is now necessary to make sure by re-examination that a sufficient twist has been accomplished. If this seems satisfactory more sutures should be put in to hold the gut firmly to the aponeurosis.

In examining with the finger now we find a double sphincter, the first one at the twist, the second, more an angulation than a sphincter, at the point of peritoneal fixation. A few chromic gut sutures close the portion of the remaining wound in the aponeurosis. The sphincteric action is maintained by the fibres of the rectus muscle as well as by the twist in the intestine. A large sized, rather stiff-walled rubber rectal tube, not a woven one, is now inserted about 6 inches into the intestine and is tied in place, a single light suture passing through its walls guarding against its accidental extrusion. The remainder of the wound is left open and packed with gauze while the tube is led off into a receptacle at the side of the bed. These wounds always become more or less infected, but I have encountered a true phlegmon only once and then a single incision sufficed for its drainage.

About a week after the operation the tube may be withdrawn and the redundant sigmoid burned off with the actual cautery. Anæsthesia is not necessary. Even then it will be found that repeated cauterizations will be required during the course of the healing in order to bring the intestinal mucosa to the skin level. Daily irrigations through the tube should be practiced so as to keep the patient's bowels open. The string around the lower piece of intestine should be removed in three or four days, otherwise there might be danger of complete and permanent closure and it is necessary to maintain patency here for the sake of drainage.

The control of the bowels is learned gradually by the patient, and he is assisted by a constipating diet and, for the first few weeks, small doses of deodorized tincture of opium and of subgallate of bismuth, 20 grains 3 to 5 times a day. It takes about a month for the final result to be attained, but the functional result in all uncomplicated cases will be found perfect.

TORSION OF THE GREATER OR GASTROCOLIC OMENTUM.

Complicated by Acute Appendicitis.*

W. H. Luckett, M.D.

So very little is really known of the mechanical cause of the twisting of the omentum that the report of this case is interesting and may serve to throw some light on the subject.

Less is known of the symptom-complex leading to a correct diagnosis of such torsions. This is demonstrated by the fact that in some sixty odd cases recently collected, extending over a period of twenty-seven years since 1882, when the first report was made by Oberst, only one case was diagnosed as such before the operation.

Corner and Pinches lead one to be satisfied with a diagnosis at the operating table and not a differential one beforehand.

Fuller points out the difficulty of diagnosis and says that it is not at all remarkable or strange for a torsioned omental tumor to escape detection even during a laparotomy, unless the incision happened to be made directly over the tumor.

Richardson suggests an anatomico-pathologic classification according to the point of twisting, and asks for a report of all cases with an explicit statement as to the location of the tnmor and the point of torsion. He thinks that if the possibility of torsion of the omentum be kept in mind in all cases of abdominal symptoms pointing to a strangulation a preoperative diagnosis of torsion of the omentum would become more frequent.

Weiner offers the very practical suggestion that if we cut down on a hernia that produced symptoms of strangulation and find only a strand of omentum in the canal we should investigate the intra-abdominal portion of the omentum to make sure that there is no torsion present.

Patient—H. P. F., foreman by occupation, 32 years of age, was admitted to my service at the Harlem Hospital, June 14, 1906.

Previous History—The patient had an attack similar to the present one two years ago, from which he recovered. He was operated on ten years ago for right inguinal hernia.

Present Illness—Two days previous to admission he was seized with very severe pains in the right iliac region, which continued unabated up to that time. He had been

Specimen showing torsion of omentum and small band of adhesion at one end.

constipated since the beginning of the attack. There was no vomiting. He was in great pain on admission. His temperature on admission was 103 F. pulse 120, respiration 26

Physical Examination—General appearance: a well-developed, conscious male, very obese. Eyes: pupils contracted but reacted naturally; mucous membrane red and dry; lips scarlet; pulse regular in force and frequency; very rapid; respiration shallow and jerky; abdomen rigid and tense, general tenderness, tympanitis, pain more marked on right side. Urine: albumin with casts, hyalin, granular and epithelial. Arteriosclerosis was present. An indistinct mass could be made out to the right of the umbilicus, reaching down into the right iliac region. A cicatrix in the right inguinal region indicated that an operation for hernia had been performed. The wound had apparently healed by primary union, and there were no signs of recurrence. A diagnosis of appendicitis was made. A high leucocytosis and differential blood-count, with the mass and other symptoms suggested abscess.

Operation—A long incision was made through the deep fascia on the outer edge of the right rectus muscle over the tumor. A quantity of bloody fluid escaped and a large mass of congested and partially strangulated omentum immediately presented itself in the wound, and was found to be adherent beneath the hernial cicatrix by the small thin band of adhesion at the lower end of the specimen seen in the illustration.

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This and several other small bands of newly formed inflammatory adhesions were easily broken up; as they were so small they were not ligated. The omentum was delivered through the wound and excised near the transverse colon. The appendix, which was found to be very markedly congested, was removed. There were, however, no adhesions between the omentum and the appendix. The abdomen was closed without drainage, and the patient left the operating room in good condition. June 18, four days after the operation, the wound was dressed and was found dry and clean. June 30 the patient was up and well.

Examination of Specimens—The specimen of the appendix was small; there were no adhesions, thought it was markedly congested, but probably not enough to account for the high temperature, pulse and leucocyte count, and surely not for the general congestion and the fluid in the abdomen.

The specimen of the omentum (see illustration) was 17 inches long, weight 9¾ ounces, and had 27 distinct complete twists or turns, the reverse to the thread of a right-hand screw. When partly untwisted it was found that the small band of adhesion to the peritoneal side of the hernia cicatrix probably came off from the lower right-hand corner of the omentum. The twists or turns as counted commenced near the attachment of the omentum to the transverse colon and ran all the way down the entire length of the omentum to the small band of adhesion to the hernial cicatrix

With a few more twists the small band of adhesion would have parted and I should have reported this case as a pure intra-abdominal torsion without adhesions or the presence of a hernia. The result of hernia operation ten years ago was perfect, and excepting the small spot to which the band was attached the peritoneum beneath the hernia scar was perfectly smooth, as demonstrated by palpation within the abdomen. Evidently a small tip of the omentum had either been ligated with the hernial sac, or the omentum had subsequently become adherent at this point, thus affording a diagonal line from the upper left corner of the omentum at the transverse colon to the lower right hand corner of the omentum, around which the free lower left irregular triangle could and probably did revolve. If the adhesion played a rôle in the torsion it does not seem possible for such adhesion at the lower right border of the omentum to have been present for ten years without giving rise to an earlier twisting. Surely the torsion could not have been present for ten years, for there would have been adhesions between the twists that would have prevented the untwisting, which was fairly easily accomplished If the adhesion was present for ten years without torsion, then some other force was necessary for its production Was it the acute attack of appendicitis? The omentum has a habit of enfolding the appendix during certain inflammations. Was it making violent efforts to get to the appendix, or was the twisting a result of a purely exterior force such as the peristaltic wave of the intestines particularly imparted by the ileum, over which the omentum lay, just before it entered the cecum? The ileum at this point being more or less fixed, the propulsive effort is constantly in the same direction from the left to the right, and the direction of the twists in my specimen of omentum are the same as would be expected if this was the case Now, the twists once started and the resulting inflammation in the omentum commenced, the increasing length of the inflamed veins would themselves tend to wrap around a line between two more or less fixed points The swelling, edema and extravasation of the blood-cells would for the same reason also augment the twisting force

Now let us go a step further. Nearly every case of reported torsion of the omentum was accompanied by some form of inflammation, either within or without the abdomen, as in a hernia. Was the inflammation the cause or the result of the torsion? The structure of the omentum has for its chief framework its vessels, long thin arteries that come off for the most part from the gastro-epiploic arteries at the great curvature of the stomach, and run downward to the lower border of the omentum, and then turn upward in the posterior layer to anastomose with the arteries of the colon. The veins are about the same. Enlarged full veins have been characteristic of the specimens of torsion of the omentum. Now the veins increase in size and length more rapidly in inflammation than the arteries, and would have a natural tendency to wrap around the latter and carry the loose mesothelium, and may perhaps be the chief factor in the production of torsion of the omentum; and I think also that we can add to this the force of the pulsations of the omental arteries.

I have suggested the foregoing, for I have long felt that the torsion of the omentum was not due wholly to exterior forces, and I believe that we must look for a cause within the omentum itself that would produce or is capable of producing torsion, because in pure hernial torsion of the omentum where the omentum is in contact with only the smooth wall of the sac it seems as if the possibility of an exterior force is negative.

INTESTINAL DIVERTICULA.*

A Pathological and Clinical Study.

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The condition known as diverticulum of the intestine has been recognized as a pathological entity for more than a hundred years, but knowledge of its relation to perforative peritonitis is of recent date, and up to the present time few cases have been operated upon in which a pre-operative diagnosis was made. Cases, however, in which this condition proved to be the underlying cause of a peritoneal infection have multiplied of late, so that its complete analysis is a matter of interest, both to the scientific investigator and to the practical physician and surgeon.

The term diverticulum of the intestine may be applied to any outgrowth of the intestinal wall, not neoplastic in character, which has had at some time a lumen connecting it with the intestine, and whose walls are composed of structures similar to those found in the intestines. Under this definition, Meckel's diverticulum is included as a congenital anomaly, and the appendix vermiformis as a normal vestigial diverticulum. When the outgrowth is composed of all the structures which are found in the normal intestinal wall, it is called a true diverticulum. When some of these structures are absent, it is called a false diverticulum. That the former may become the latter, must be recognized.

The older classification into congenital and acquired diverticulum serves no useful purpose, and should be discarded, because with our present knowledge we can draw no distinguishing line between the two, except in the case of Meckel's diverticulum and the appendix; and we believe, as will develop later, that most, if not all, cases of diverticula have at least a congenital predisposition.

The structure of a diverticulum, when not inflamed, is very simple. If of the true variety, it is nothing other than the pouching out of the intestinal wall at some point. A section across the pouch shows the same coats arranged in the same way as in that part of the intestine of which it is an outgrowth. If of the false variety, the individual coats are more or less modified, and there is a practical absence of one or more of them, usually of the two muscular layers. In their early development, they are microscopical in size, Graser (1), Fischer (2), and show at this time the characteristics of the true diverticulum. With their growth, however, the false characteristics come into evidence. If no inflammation supervenes, the structure remains unchanged during a considerable growth, so that the diverticula, varying in size from a buckshot to a hen's egg, may be seen presenting the simple structure above described. On the other hand, a varying amount of atrophy, particularly of the mucosa, may take place, and a hypertrophy of the submucosa and the subserosa. These changes are not, properly speaking, inflammatory, but are due to pressure. If no further alteration take place these diverticula do not give evidence of their presence by any clinical symptoms, in this respect resembling a Meckel's diverticulum and the appendix vermiformis. If, on the other hand, inflammatory changes do take place, there are present exactly the same factors for producing mischief as exist in the appendix and Meckel's pouch.

Until recent years it was believed that these diverticula are rare. Now, however, they are known to be common, and with this knowledge has come the further knowledge that they are the seat of great potential danger to health and life. In making a systematic search, Graser found 10 cases in 28 autopsies; Sudsuki (3) found 15 in 40 autopsies; Stierlin (quoted by Verdenal [4]) found 10 in 38 autopsies. These were all in the lower colon or sigmoid. Baldwin (5) has found 14 diverticula of the

* Reprinted from the Americal Journal of Medical Sciences, August, 1910.

duodenum in a systematic search of 104 cadavers in the anatomical room of the Cornell Medical School. In 81 autopsies done at the Presbyterian Hospital, in New York City, from June, 1909, to February, 1910, 5 cases of sigmoid- and colon-diverticula are recorded, all of a well marked size.

Intestinal diverticula have been found in every portion of the alimentary tract, from the pylorus to the anal ring. The duodenum has furnished a large number (Baldwin); the whole small intestine has shown them; the appendix vermiformis itself has not escaped, Fischer Mertens (6), and they have been found in large num-

Figure 1.—Diverticula of the small intestine. The diverticula all occur along the mesenteric attachment. (Case XVIII.)

bers in the colon and the sigmoid. The infection producing ischio-rectal abscess may find its way from the bowels through a diverticulum, Chiari (7), though the latter is rare in the lower rectum. Apparently the sigmoid is the favorite site for their development. This may be accounted for by the fact that the secondary causes in their production, as elaborated later, are more potent here than in other parts of the bowel.

Their comparative absence in the rectum proper is interesting and is ascribed by Schreiber (8) to the better musculature in this part. The total number found in one person may run high up in the hundreds. Structurally, they are the same no matter in what portion of the canal they are found, and there is no evidence that the etiological factors differ. In looking for their cause, therefore, we must accept only such conditions as are present along the whole intestinal tract, and such factors as do not conform to this condition must be excluded as primary causes.

A very large proportion of the diverticula of the small intestine occur either between the mesenteric leaves or close to them (Fig. 1), and this fact led to the belief that there existed an inherent weakness here which was responsible for the hernial protrusion. The colon, however, often shows them placed laterally (Fig. 2). Herczel (9) and Good (10) showed that bulging of the intestinal wall first took place at the mesenteric border when the dead intestine was subjected to increased pressure within its lumen by distention with water. Hansemann (11) succeeded in producing actual diverticula. It was noted, however, that the weakness was present only in old persons, and not in children. Klebs, quoted by Beer in a study of diverticula, first noted that the protrusion bore a close relation to the blood vessels entering and leaving the gut along the mesenteric attachment. This fact has been corroborated by every subsequent observer, and it was noted that the same relation held in the artificially produced bulgings.

These pathological and experimental findings were made the basis of a full explanation of the etiology of diverticula, as follows: The mesenteric border is weak;

it is weakest at the point of entrance and exit of the vessels, particularly the latter; this weakness naturally increases with age; a comparatively moderate increase in internal pressure determines the giving away of the wall at one of these points, and the diverticulum is an accomplished fact. The constipation of the old was given as the cause of the increase in pressure. This explanation was complete for the condition as then understood. Further consideration, however, throws much doubt on it. Chlumsky (12) showed that no conclusions drawn from experiments on the dead gut were admissible as explaining facts existent in the living gut. He experimented with the normal intestine in the living dog, and with the intestine ten hours after death. In the former the rupture took place invariably opposite the mesentery, while in the latter, along the mesenteric border. Moreover, Philipowitz (13) demonstrated that the dead intestine ruptured long before it had been distended to anything like the extent seen in the living subject in volvulus and other forms of obstruction. Beer (14) quotes these findings and uses them as arguments against the suposed inherent weakness along the mesentery. He further calls attention to the fact that clinically, rupture of the intestine, from whatever cause, almost invariably occurs opposite the mesentery. He explains the difference in the results in the living and in the dead intestine as due in the first instance to the pressure of the blood stream filling the vessels and thus closing the spaces of entrance and exit, while in the latter, that is, the dead gut, the empty vessels leave a place of lessened resistance around them. He says: "The supposed weakness of the mesentery—in the living intestine—does not exist, and as it does not exist, it has nothing to do with the origin of acquired diverticula."

Graser investigated the subject most thoroughly as applied to diverticula occurring in the sigmoid. He found the same relation to the vessels as other observers; that is, the hernial protrusion follows the emerging vein and often takes a wandering course through the intestinal wall, finally to reach the subserosa.

In this passage the circular muscular coat first gives away and the longitudinal follows later, or may only be thinned out. He then sought for the actual cause of the diverticulum and thought he found it in the presence of any obstructive lesion to the free return of blood through the inferior mesenteric vein, particularly where, as in valvular heart lesions, the interference might be remittent. Under these conditions

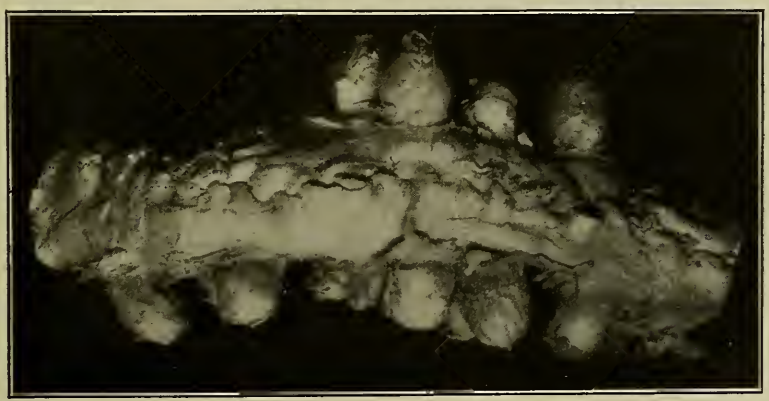

Figure 2.—Diverticula of the colon. The diverticula lie between the lateral teniæ and the mesenteric attachment. (Case XVII.)

when the obstruction is marked the spaces through which the veins pass are dilated and the connective tissue and muscular bundles weakened. With the comparative collapse of the veins, when a free circulation is reëstablished, the spaces present a point of lowered resistance, and a gas or liquid pressure from within starts the development of the diverticulum. By a careful study of twenty-eight cases, from which he made over a thousand sections, in series, he believed he fully established this relation. He, however, pointed out the fact that the circulatory disturbance was only a predisposing cause, and that diverticula were not necessarily present in every case having such a disturbance.

Graser's view was opposed at the time he presented it, by Hansemann and others, and a year later Sudsuki made a study to prove its error. He examined, postmortem, twenty-eight sigmoids taken from patients who in life had suffered from interference with the venous return in the region of the inferior mesenteric vein, and found diver-

ticula present in six of them. On the other hand, in twelve cases in which no evidence of such an interference existed, he found diverticula present nine times. He further showed that the size of the vein sheaths was independent of any obstructive lesion during life, the space often being distinctly larger when no such obstruction existed than it was in those cases in which it did exist. He concludes that Graser's findings were purely accidental, and that no causative relation exists between a circulatory disturbance and a diverticulum. He believed that the venous sheaths may be a point of weakness because of the thinning out of the connective tissue support in the subserosa and submucosa. This weakened point then gives way under the pressure of gas and feces, and the diverticulum results. Probably in the beginning it is of the true variety, but later the muscular coats give way, and it becomes false in character.

This explanation of the etiology may be accepted, in part at least; for those di-

Figure 3.—Piece of colon obtained from a boy, aged six years. In one of the haustra, two diverticula can be seen, one on either side of the anterior tenia. (Case VII.)

verticula which are found near the mesentery where the veins are emerging, but, as Beer points out, it does not hold for those which occur on the convex side of the bowel. He, therefore, only accepts the weakening of the wall due to the passage of vessels through it as of secondary importance in a causative way. He offers the following explanation of the cause of diverticula: "There must be some change in the resistant powers of the gut wall. The fact that diverticula occur in old people, in people whose intestines have been more or less worked out, as evidenced by constipation, points to a muscular deficiency, and in this muscular weakness, the cause of the formation of false diverticula must be sought." . . . "It is very probable that the original view of Klebs is, in part, correct, especially with reference to the production of the diverticula in the small intestine, and that traction on the gut by the mesentery is a factor in the production of the necessary weakness at this point, where these diverticula so regularly occur in the small intestine. That this traction is a reality can be easily demonstrated by distending loops of intestine *in situ,* or by noting the enormous tension of the mesentery in ileus cases. Naturally, in those parts of the intestine where no mesentery exists, this cannot be a factor."

That Beer's view is correct, so far as the pathological changes which lead to the diverticulum are concerned, we are willing to accept; but that he is incorrect in the primary cause of this change, namely, weakened musculature, due to age, is manifest from the fact that diverticula are found in children and young adults.

Ashhurst (15) has reported a case in a boy of seven, and two of the cases reported in the present series occurred in children of seven and ten years, respectively (Figs. 3 and 4). A number were found in persons under thirty. In none of these was there clinical evidence of deficient muscular activity of the intestine. The following observation, too, is of value in this connection. An examination of the colon from five infants who had died from various infantile diseases was made for the purpose of demonstrating the presence or absence of points of weakness in their walls. The colons were moderately hardened in formalin, and then filled with water just

sufficient to render the walls taut, but not under enough pressure to stretch them. In three of the cases there was some evidence of a weakness at one or more points, while in two such evidence was absent. In each of the positive cases there occurred a slight outpushing of the wall of the intestine, about 1 cm. in diameter, which had somewhat the macroscopic appearance of the small diverticula seen in adults. The wall over the fundus of the sac seemed to inspection and palpation distinctly thinner than in other parts of the gut. Microscopically, in sections taken transversely through the guts at the points described above, the muscularis appears definitely thinner than in the adjacent gut wall.

We, therefore, are driven to the conclusion that up to the present time no complete explanation of the primary cause of intestinal diverticula has been offered. The most that can be said is, that from some cause a weakness exists in the intestinal coats, and by reason of this weakness, a pouching of the coats takes place when any undue pressure arises. Conditions such as age, constipated habit, excessive fat or emaciation, portal congestion, the anatomical weakness at the point of entrance or exit of vessels all play an undoubted role, but they are probably secondary to the inherent weakness above mentioned. Telling (16), in a very able discussion of the condition, based on a study of 105 cases, leaves the question of etiology unsettled. In speaking of this, he asks: "In answer to this question, it is significant that no case has been reported in a child (Hale White, Schreiber)—(this we now see is incorrect)—while the great majority are in the old, even aged, subjects. Moreover, the various points which have been successively established with regard to their etiology would seem to put the answers to this question beyond doubt, even though we admit that a congenital anatomical arrangement of the muscle fibres, or of the connective tissue of the vessel spaces of the gut wall furnishes a special predisposition." "Whether this muscular weakness and thinning is a constant or frequent accompaniment, or whether it is a congenital or acquired condition are points on which further research is needed."

It seems to us that great stress should be laid on the probability that a congenital defect in the musculature does exist, and that most diverticula occur because of this defect. Contrary to the expressed view, that young persons are not subject to them,

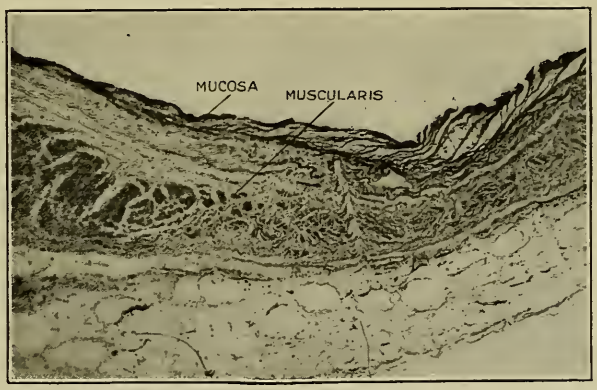

Fig. 4.—Microscopic section through a diverticulum in the sigmoid of a girl, aged ten years. The mucosa is flattened. The muscularis becomes thin and atrophic, almost disappearing over the fundus of the sac. (Case VIII.)

as we have stated, there are many recorded cases in patients under thirty, and not a few in young children. Moreover, Edel (17), Fischer, and others, as well as the specimens here presented, give strong evidence that in the first stage all diverticula are of the true type, and that only subsequent pressure destroys the muscular coats, showing that the muscular coats previously exhibited a weakened condition. The conditions found in the infant colons above referred to is very significant in this connection.

The pathology of intestinal diverticulum needs to be considered under two distinct conditions: its pathology when uncomplicated by secondary changes, and the pathology when such changes have intervened. A detailed study of this has been made by us on the material at our disposal, and is reported in full. Emphasis will be laid at this time only on those points which are of clinical significance.

It must be borne in mind that the diverticulum itself is absolutely a harmless condition as far as the health of the individual is concerned. Of the specimens re-

ported in this paper, eighteen in number, four were the cause of symptoms during life. In each one of these the symptoms were due, not to the actual diverticulum, but to the secondary changes occurring from it. Telling names eleven possible conditions which may give rise to symptoms, and illustrates each one of them by one or more of the cases which he summarizes. Some of these are so nearly related, the one to the other that they may be considered modifications of the same process, and their separation seems to confuse rather than to simplify. A practical working classification of the secondary changes which give rise to symptoms is one which is in every way comparable to those occurring in the case of the appendix.

1. There may arise an acute inflammation of the diverticulum without perforation which results in a peritonitis or a cellulitis around it. Loomis (18) reports one case in which general peritonitis so resulted. The formation of adhesions to neighboring parts may cause an obstruction, more or less acute, either at the site of the diverticulum or in a loop of gut adjacent to it.

2. The inflammatory process may cause destruction of the coats of the diverticulum when a perforation results, leading either to a localized abscess, a general peritonitis, a general blood infection, or all three. The perforation may communicate with other hollow viscera, notably the bladder. Telling cites a case showing submucous perforations, so that fistulous tracts formed within the intestinal wall.

3. The diverticula may become the seat of a mild, subacute, or chronic inflammation, which does not produce marked changes. This condition is subject to temporary exacerbations and remissions. (Giffin (19) Mayo.)

4. A chronic inflammation may occur in the diverticulum which leads to thickening of the walls of the diverticulum itself, and from the irritating effect of the toxins in the lymphatics and venules, the process spreads to the surrounding tissues, resulting in thickening of the whole intestinal wall and of its mesentery. When multiple diverticula are present, a long piece of the gut may be involved. Here, again, adhesions may lead to intestinal obstruction, or this obstruction may result from narrowing of the lumen. Here, also, a chronic perforation may take place.

5. Carcinoma may develop on the diverticulum, Hochenegg (20), Wilson and Giffin (21).

Comparing these changes with those of the diseased appendix, we find them exactly analogous: that is, acute inflammation without perforation; acute inflammation with perforation; subacute and chronic inflammation without marked thickening; chronic inflammation with marked thickening; and carcinomatous development. The question naturally arises as to what is the cause of these changes. In the majority of cases they are probably due to the irritation caused by the fecal concretions in the intestines. For this reason the secondary changes are almost invariably found in the large intestinal diverticulum, where the solid feces become impacted in its lumen.

Gordinier and Sampson (22) report one case of inflammatory changes in a mesenteric cyst of the small intestine, with the presence of many diverticula in the adjoining intestine. But they fail to give microscopic evidence that the cyst was actually developed from a diverticulum.

The analogy between the causative factor in diverticulitis and appendicitis is again close, namely, irritation from fecal concretion. On the other hand, owing to the motility of the appendix on its mesenteric axis, it is liable to serious damage from circulatory disturbance which is not present in the case of the diverticulum. Consequently, acute gangrenous appendicitis is common, but acute gangrene of a diverticulum as a whole probably never occurs. Another distinguishing difference is, that inflammatory changes in the appendix usually involve the mucous membrane to a marked degree, while the mucous membrane lining the diverticulum often escapes until actual perforation is imminent. Wilson discusses this, and would restrict the term "diverticulitis" to those cases in which the mucosa is primarily involved, and use the term "peridiverticulitis" for those cases in which the outer coats of the bowel and surrounding structures are inflamed. The former causes no material reduction of the lumen of the bowel, but tends to perforation into the peritoneal cavity. The latter produces a marked narrowing of the lumen, but owing to the marked reparative process, does not so readily lead to perforation. This distinction of terms seems to us rather superfluous, because the subserosa is quite as much a part of the diverticulum as is the mucosa. Moreover, in many of the cases in which perforation has been reported clinically a condition of "peridiverticulitis" did exist. It is also important to note that the inflammatory changes in diverticula are most marked in the connective tissue coats of its wall, the submucosa and the subserosa.

For this reason it is probable that the acute perforations result in chronically inflamed diverticula, and that the acute inflammations themselves are usually superadded upon a chronic inflammation. The tendency of a perforation of the diverticulum to

communicate with the bladder is worthy of emphasis. Formerly these communications between the sigmoid and the bladder were attributed mostly to cancer, but Harrison Cripps (23) collected sixty-five cases of vesicocolic fistula, in forty-five of which an inflammatory process was shown to be the underlying cause, as against nine in which cancer was so related.

The clinical manifestations of these conditions are readily understood by a direct application of these pathological changes.

It must again be emphasized that the diverticulum itself, that is, a pouch of the intestinal wall, is not capable of giving symptoms. It is only when added to this, there exist some of the secondary changes above described that the symptoms rise. Autopsy records show the frequent presence of diverticula which, even when packed full of

Fig. 5.—Diverticula of the colon. The diverticulum is stuffed with feces. (Case XI.)

feces during life, have given no hint of their presence (Fig. 5). Moreover, a very considerable degree of inflammation in the diverticulum, and in the immediate vicinity, may be present without giving symptoms. This is well illustrated in one of the clinical cases in this series in which a chronic perforation took place with no accompanying signs until the moment of perforation.

On the other hand, there may be evidences of the secondary changes present during the chronic stage. These are: disturbance of the action of the bowels, usually constipation, and possibly a dull aching pain.

These cases may recover spontaneously, according to Mayo (24), and he reports a case in which recurrent symptoms had been present over a period of years. Here, again, we see an analogy to appendicitis.

There are no symptoms referable to the varying inflammatory conditions that are in any way pathognomonic. The same clinical picture is seen when similar pathological processes are present from other causes. For this reason, rarely, if ever, has a positive preoperative diagnosis been made, and an error is not infrequent, even on opening the abdomen. However, certain symptoms are significant, and with our increasing knowledge, errors both before and during operation will become more infrequent.

The predilection of the descending colon and sigmoid to be the seat of serious changes in diverticula, leads at once to a tentative diagnosis of this condition when evidence of acute or chronic inflammation exists in the left lower quadrant of the abdomen. (One of our clinical cases, however, was in the ascending colon.) This, occurring in persons in the middle decades of life, is sufficient to suggest a diverticulum as the starting point of the trouble, but it must be emphasized that an increasing number of cases showing inflammatory symptoms are being found in young persons. The symptoms may be those of a local abscess, a more or less general peritonitis, or a partial or complete intestinal obstruction. They may be acute, subacute, or chronic. Owing to the absence of ulcerative changes in the mucous membrane, diarrhœa and blood in the stools are the exception, though the latter existed in the case of Moschcovitz, the specimen from which is included in this series. The usual absence of these symptoms helps to differentiate the condition from tuberculous inflammations, and to a certain extent, from syphilitic inflammation and carcinoma.

In those cases in which the inflammatory exudate is extensive, leading, as it may, to a palpable tumor, there are no clinical manifestations which differ from a similar

condition due to other causes. The absence of other evidence of tuberculosis or syphilis, and the absence of blood in the stools, all point to the presence of diverticular trouble, but a positive diagnosis cannot be made. The greatest difficulty exists under some circumstances in excluding carcinoma of the sigmoid. The resemblance to this neoplasm is so close that many surgeons have been in error after opening the abdomen, the thickened indurated section of the gut being in every way the same in both processes, and primary resection has been done because of the mistaken diagnosis. Telling, in his pathological classification, gives as one type those mimicking carcinoma, and adds that he believes that many an inflammatory lesion would be found to be present in jars on museum shelves labelled "carcinoma," if their contents were carefully examined.

Moynihan (25) reports five cases in which a resection was done in the erroneous belief that cancer was present. In two of these the lesion was positively demonstrated to be due to diverticular inflammation. In a sixth case the indurated colon and sigmoid were believed to be the result of cancer, and the case was considerd inoperable. The subsequent recovery proved the error of this diagnosis, and the case probably should be included as diverticulum disease. An enterovesical fistula, with gas or fecal matter passing out with the urine, points to a diverticulum rather than to cancer. Thus we see that, clinically, we recognize a classification which conforms in every particular with that adopted for the secondary pathological changes.

Beer, Telling, Eisendrath (26) and others have formulated tables of such classification, which possess merit. However, an understanding of the possible anatomical lesions serves every purpose, and since all these lesions have now been reported clinically, a table of clinical possibilities is nothing more than a repetition.

The treatment for the secondary changes growing out of the presence of diverticula, except the milder grades of chronic inflammation, is purely operative. A laparotomy must be performed, and the actual condition met with must be treated on the general principles of intestinal surgery. In the case of a perforation, it may be dealt with by simple excision of the necrosed area, and suture, or a section of gut may be excised and an anastomosis done. The latter is only needed when the perforation is large, and the adjacent gut wall is so thickened that a proper closure cannot be effected.

A second indication for excision of the gut is the narrowing of the lumen by inflammatory thickening to a point which threatens its patency. But in this connection it must be remembered that much of the inflammatory exudate may be absorbed when the exciting cause, namely, the inflamed diverticulum itself, is removed. On the other hand, we must bear in mind the possibility of more than one diverticulum being present, so that a proper attention to the perforation, or the most apparent pouch, may not remove the causes exciting inflammation. Again, the possibility of the development of cancer as a subsequent change must be given its full weight in deciding against intestinal resection.

The surgical management of the local abscess, the general peritonitis, the adhesive ileus, or the fistulous opening into the bladder is exactly similar to these conditions from other causes and needs no amplification here.

The following clinical cases and postmortem specimens illustrate many of the facts included in the foregoing *resume*. The clinical cases have all been presented before the New York Surgical Society during the session of 1909-1910. So far as we know, none of the other cases have been previously reported.

Case I (Hartwell, Presbyterian Hospital)—O. G., male, aged forty-two years, mechanic; was admitted to the Presbyterian Hospital, in the service of Dr. Eliot, to whim I am indebted for the privilege of reporting the case, on April 21, 1909, suffering from an acute abdominal lesion. The family and past history were negative. Two days before admission he developed the typical symptoms of an acute intestinal obstruction, and these had increased continuously until admission. For three or four days prior to the acute symptoms he had noticed that his bowels were constipated—an entirely unusual thing.

Physical examination on admission showed the abdomen uniformly distended and tympanitic. About one inch inside the anterior spine of the ileum, and above it, was felt an elongated mass along the course of the sigmoid, the size of an apple. This mass was tender. Careful questioning failed to get any evidence that the patient had ever been conscious of any abdominal lesion prior to the onset of the acute symptoms. With these, however, the pain was most severe at first at the site of the tumor.

Under gas-and-ether anesthesia a laparotomy was immediately done, the peritoneum being opened over the mass. A walled-off abscess was found lying outside the sigmoid, just above the pelvic brim, which communicated with the lumen of the bowel through a gangrenous looking perforation. For a distance of about two inches the

entire bowel wall was markedly thickened, as was the mesentery connected with it. There were two adhesion bands kinking and pressing on the gut in such a way as to cause the obstruction, but it was noted that the colon, as far as could be seen above this point, was not unduly distended. No diagnosis was made as to the pathology of the lesion. Cancer and tuberculosis were thought of as the most probable, though diverticulitis also was mentioned. A primary resection of the diseased portion was done, with an end-to-end suture anastomosis. The abdominal wound was sutured with drainage.

Fig. 6.—Part of the sigmoid. On the right is an indurated mass of inflammatory tissue, laid open along the tract of the perforating diverticulum. (Case I.)

The post-operative course was unsatisfactory, and the symptoms of obstruction increased rather than lessened. After twenty-four hours, therefore, the wound was opened, and as the anastomosis did not look entirely satisfactory, though the lumen was patent, the stitches were removed and a Murphy button inserted. The patient recovered after a rather tedious convalescence, and has remained well up to present time.

The specimen removed consists of a piece of sigmoid 7 cm. long (Fig. 6). The peritoneal fat and appendices epiploicæ are abundant. On the external aspect of the section is an indurated mass, irregularly globular, measuring 4 to 6 cm. in diameter. This mass lies within the gut wall and is covered externally with peritoneum and intestinal fat. Through this mass passes a perforation into the intestinal lumen, admitting a surgical probe. The surface of this sinus is ragged and ulcerated. The perforation passes through the posterior part of the mass, and a transverse section through the mass shows the mucous membrane pouching out along the line of the perforation, demonstrating the presence of a diverticulum at this point. There are four other diverticula present, having an average depth of ½ cm.; two of those lying adjacent to the one that has perforated show a lesser amount of induration in their walls. Microscopically (27), a section taken through the tract of the perforation shows extensive necrosis and acute inflammatory changes involving all the coats of the gut (Fig. 7). At one place the mucosa dips down as if to form a diverticulum, but becomes almost at once unrecognizable in a mass of necrotic tissue. This necrosis involves the muscularis, which is considerably thinned out at this point, as well as the subperitoneal fat tissue. The parts surrounding the necrosis are densely infiltrated with polymorphonuclear leukocytes and lymphoid cells. Sections through two of the adjacent diverticula shows both of them to be true diverticula, being surrounded by normal muscularis of the usual thickness. The subserosa contains many lymphoid cells, with a few polynuclear leukocytes. Both of these diverticula are more or less cylindrical in shape, main-

taining about the same diameter throughout their entire length. The deeper one measures 1.2 cm. in length; the other, 0.7 cm.

Case II (Hartwell)—Male, 23 years of age. Admitted to the Presbyterian Hospital August 9, 1909, giving a complicated clinical picture, which is reported in full elsewhere (28). He presented at operation the following condition: The abdomen contained a small amount of fluid, of characteristic serous exudate. The large intestine, from the splenic flexure to the rectum proper, was found to be the seat of a marked uniform thickening, involving its whole circumference. This wall was estimated to be about ¾ inch in thickness, so that the intestinal tube was rigid and hard,

Figure 7.—Microscopic section through a perforating sinus. The section shows the mucosa abruptly terminating in a mass of necrotic tissue. The wall of the gut is thickened and infiltrated with leukocytes. (Case I.)

but its lumen was not appreciably narrowed. At the splenic flexure the lesion had, to a certain extent, kinked the bowel, causing a moderate degree of obstruction. The mesentery of the descending colon was thickened quite as much as the bowel itself. The spleen was soft and somewhat enlarged. No other lesions were found in the peritoneal cavity, a thorough examination being made to find tuberculosis, but without avail. The adhesions which were causing the obstruction were loosened, and the whole length of the descending colon was examined for the purpose of finding a perforation or any other cause for the condition at hand. The process gave all the appearances of a simple inflammatory thickening, involving the bowel and its mesentery. It was impossible to eradicate the disease consequently the abdomen was closed with drainage. A pathological report on the peritoneal fluid showed it to be sterile.

A microscopical examination of a small piece of the tissue removed from the surface of the bowel showed it to be fat, infiltrated with small round cells, and extravasated blood. There was an increase of fibrous tissue and the walls of the bloodvessels were thickened, and the lumen contracted. There was no special perivascular change, and no evidence of either syphilis or tuberculosis could be found. The diagnosis made by the pathologist was chronic fibrous peritonitis.

The postoperative history was uneventful. There was but little drainage from the wound, and it healed kindly. Since his discharge from the hospital on September 10, the patient has been attending to his work, and is in very excellent general health. There is still present a mass in the left lower abdomen, which is not materially changed since the operation, but it gives rise to no symptoms whatever. All the evidence at our disposal points to the condition of the colon as being one of a simple inflamma-

tory process involving the coats outside of the mucous membrane. Tuberculosis and syphilis both involve the mucous membrane, and give symptoms of this involvement. Cancer must be ruled out by the extent of the disease, and the subsequent good health of the patient. On the other hand, such inflammatory thickening arises from diverticulitis, as has been amply demonstrated, both by previous writers and by the specimens here presented, and we therefore think that it is proper to include the case as one of probable multiple diverticulitis. In this connection Telling states that he has found the thickening to be more marked in those diverticula with small openings, and narrow channels. Such diverticula cannot be demonstrated from the external surface of the thickened bowel.

Case I showed the same condition in a local area, but here a perforation was also present. These are the cases that give the mimicry of cancer.

Case III (Hartwell)—A. G., female, 43 years of age. Admitted to the Presbyterian Hospital, August 30, 1909. For ten years she had suffered from recurring attacks of abdominal pain, coming on at night and being relieved by vomiting. The pain was general, but was most severe in the epigastrium. Two years prior to admission into the hospital the pain began to localize itself in the right lower quadrant of the abdomen. With the attacks there was fever. They recurred every three or four months, and lasted about one week. She habitually suffered from constipation. There was never any knowledge of blood in the stools. The physical examination showed no abnormalities except some evidence of a chronic pelvic peritonitis, and a mass in the right lower quadrant of the abdomen. This was about the size of a billiard ball, of stony hardness, and fairly smooth surface. It was tender to pressure. It occupied the middle outer part of the quadrant, and was firmly adherent to the posterior abdominal parieties.

Operation was performed on September 12. On opening the peritoneum the mass was found to lie just outside the cecum, and to consist of the appendix, the cecal wall, and adventitious tissue. The appendix was much thickened, but not acutely inflamed. It lay with the tip pointing upward, outside of the cecum, buried in hard

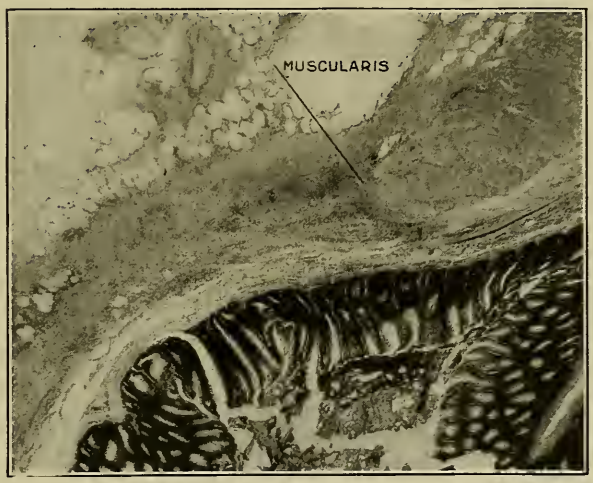

Figure 8.—Microscopic section through a diverticulum. (Only half of the diverticulum is shown.) The muscularis ends abruptly at the neck of the sac. The wall of sac is composed of mucosa and serosa. The latter is infiltrated with leukocytes. (Case III.)

tissue. On dissecting it free, the tip was found to be closely adherent to the colon, just anterior to the outer mesenteric leaf, where it closed a necrotic opening 0.5 cm. in diameter in the much thickened and hard wall of the colon. This opening admitted a probe into the lumen of the bowel. The appendix was removed. The tissue for some distance around the sinus was cut away in two pieces, and the opening thus made closed with three layers of sutures. The lumen of the colon and cecum contained old, partially digested blood clots, the origin of which could not be determined.

The post-operative course was uneventful, and the patient remains well at the present time.

The specimen consists of: (1) Two pieces of intestinal wall (cecum), both of which show considerable thickening. In one of the pieces there is a small saccule, 8 mm. in diameter and 9 mm. in depth, lined with mucous membrane, which appears to have pushed through the muscularis. (2) An appendix, 4 cm. in length; serosa of distal portion covered with fibrin; no perforation; mucosa smooth. Microscopically: (1) Sections taken through the diverticulum show a small sac lined with intestinal mucosa, which is thrown up into small folds. At one point the mucosa is necrotic. The lumen of the sac contains pus. The wall of the sac is composed of fibrous tissue, apparently thickened serosa, infiltrated with polymorphonuclear leukocytes and lymphoid cells, but free from necrosis. No muscular tissue remains in the wall. Its blunt point of termination on either side of the sac is sharply defined (Fig. 8). The terminal muscle fibers show signs of atrophy and are being replaced by fibrous tissue. (2) Sections through the cecum adjacent to the diverticulum show considerable thickening of the muscularis and serosa and a universal infiltration by polymorphonuclear leukocytes, lymphoid and plasma cells in all the coats. There is a formation of fresh granulation tissue on the serosa. (3) Appendix. The mucosa is intact. The muscularis and serosa contain a moderate number of lymphoid cells. The serosa is thickened. Our interpretation of this case is that the cecum contained a number of diverticula. One of these had perforated and sloughed away. A second one, acutely inflamed, is the one from which the above described section was taken.

Case IV (Moschcowitz)—Female, 37 years of age. This patient had suffered from a number of conditions requiring surgical attention in earlier life. Among these was an acute appendicitis, for which she was operated on in 1904, and gastric ulcer, which was cured without operation. In 1905 she first began to suffer from intestinal trouble, which manifested itself by diarrhea, tenesmus, and blood in the stools. Examination then showed a tender sausage-shaped mass in the left iliac fossa. In June, 1906 she was operated on, and a condition of retraction and contraction of the mesosigmoid, with many scar-like adhesions taking their origin from multiple diverticula of the sigmoid, was found. Separation of the adhesions, and straightening out of the intestinal coils gave relief for about two years, when the symptoms recurred. In March, 1909, a resection of the diseased portion of the sigmoid was done, and this has resulted in a complete cure up to the present time. The specimen consists of a section of the sigmoid, 12 cm. in length, hardened in formalin. After opening along the anterior border, inspection from the inside shows fourteen diverticula. These are all small, having a communication with the intestine, 0.5 cm. in diameter, and a depth of 0.5 cm. None showed marked evidence of inflammation. In the hardened specimen there is no evidence of their presence on the peritoneal surface of the gut. The whole intestinal wall, however, seems somewhat thickened. Microscopically, a longitudinal section through one of the diverticula shows the following: The mucosa lining the saccule is normal. The submucosa shows no changes. The circular coat of the muscularis is very much thinned over the fundus of the sac. The longitudinal layer maintains its normal thickness. The submucosa contains considerable fat tissue. In the region of the diverticulum it is infiltrated with a moderate number of polymorphonuclear leukocytes and lymphoid cells. The serosa is thickened. The intestine adjacent to the diverticulum is normal.

Case V.—The patient from whom this specimen was obtained was a male, 48 years of age. He died in the Bellevue Hospital from general metastases, following an epithelioma of the œsophagus. Nothing in the history gave any indication of a lesion existing in the sigmoid. There was no evidence of any cardiac trouble nor any condition leading to portal congestion.

The specimen consists of the lower end of the sigmoid, measuring 12 cm. in length, and containing six diverticula, all of which have a long, narrow neck, barely admitting a small probe, through which they connect with the lumen of the intestine. The diverticula are spherical in shape, and measure about 0.5 cm. in diameter. They are filled with semisolid feces. The feces, owing to the narrowness of the outlet, are practically prevented from re-entrance into the lumen of the bowel. The position of the diverticula is on either side, between the anterior and lateral teniæ. In some cases the diverticulum is in close relation to an appendix epiploica. In others, no such relation can be demonstrated. The thickness of the intestinal wall is distinctly greater in that portion where the diverticula are present than in that portion where they do not exist.

Microscopically, sections taken transversely through two different diverticula present the same picture. The mucosa is thick at the neck, but becomes thinned out in the fundus. The muscularis of the adjacent gut is hypertrophied, but only a small part of the longitudinal layer passes about the diverticula, forming a thin strip of atrophied muscle between the mucosa and serosa. By the use of Van Gieson's stain, con-

siderable fibrous tissue is found between the muscle fibrillæ about the diverticulum. The subserosa contains several fairly large bloodvessels, both arteries and veins, and a considerable quantity of adipose tissue. The serosa appears normal. There is no sign of acute or chronic inflammation in any part of the saccule.

Case VI.—The specimen was removed from a male, 75 years of age, who died in the Presbyterian Hospital following a resection of the small intestine for gangrene in a strangulated hernia. The autopsy showed a general arterial sclerosis and a chronic endocarditis, but there was no evidence of congestion in the abdominal viscera. The specimen consists of a small section of the transverse colon, which presents one diverticulum. This arises from a plane midway between the anterior and one of the lateral tenia. It is exactly globular in shape, and measures 1 cm. in diameter. It communicates with the lumen of the gut by a circular opening, also 1 cm. in diameter. The sac of the diverticulum contains an elliptical enterolith about 0.5 cm. in its long axis and 0.25 cm. in its short axis. This, therefore, lies loose, and is not impacted. The walls of the diverticulum are distinctly thinner than the wall of the gut around it. This specimen was preserved intact, so that no microscopic sections were taken.

Case VII.—The specimen was obtained from a boy, 6 years of age, who died in coma in the Presbyterian Hospital from an acute infectious condition of only twenty-two hours' duration. The only abnormalities found at autopsy by the coroner were those described below, under the specimen, and a condition of ulceration in other parts of the colon and lower ileum.

The specimen consists of a piece of colon showing three haustra. Each of these is more sacculated than normal. The specimen is opened along the mesenteric line. In one of the haustra the walls are distinctly thinner than in the others, and here exist two diverticular pouches, one on either side of the anterior tenia (Fig. 3). They are exactly similar, being globular in shape, and measuring about 2 cm. in diameter. Their communication with the lumen of the gut is by a circular opening of the same diameter. The condition, therefore, is more a giving way of the whole wall of the gut in an intermuscular portion than the presence of actual diverticula. The thickness of the wall in this weakened haustra is much less than in those adjoining it.

Microscopically, a section through the diverticulum, taken longitudinally, shows a small saccule lined with flattened mucosa, but completely surrounded by a muscularis, which consists of both the circular and longitudinal layers. Both layers are considerably thinner here than in the adjacent intestine, but in all other respects they appear normal. The serosa and subserosa are normal. The intestine adjacent to the diverticulum is normal.

Case VIII.—This specimen was obtained from a female, 10 years of age, who died in the Presbyterian Hospital from a septic meningitis following otitis media. There was nothing in the history pointing to any intestinal trouble. At the autopsy nothing was found indicating any interference with the venous circulation of the abdominal viscera.

The specimen consists of a small piece of the sigmoid, which has been opened along the mesenteric line. There is one diverticulum present. Its communication with the intestine is oval, measuring 1 cm. in length and 0.5 cm. in width, the longer diameter being transverse to the axis of the gut. The pouch is about 0.5 cm. deep, and is of the same diameter as the opening into the intestine. There is no appreciable difference in the thickness of the wall of the diverticulum and that of the intestine about it. The position of the diverticulum is midway between one of the lateral tenia and the mesenteric line.

No relation to an appendix epiploica can be made out.

Microscopically, transverse sections through the diverticulum show the following changes: The mucosa lining the saccule is flattened. The submucosa is normal. The muscularis becomes rapidly thinner as it passes on to the diverticulum but does not disappear entirely (Fig. 4). Over the fundus it has been largely replaced by fibrous tissue, and it is only in sections stained by Van Gieson's method that the atrophied muscular fibers, chiefly of the longitudinal coat, can be recognized. The serosa and subserosa are normal. There are no large vessels in the wall of the sac. The intestine adjacent to the sac is normal.

Case IX.—This specimen was obtained at the autopsy in a female, 65 years of age, who died in the Presbyterian Hospital from chronic obstructive jaundice due to calculus, gangrene of the gall-bladder, and septic cholangitis. The heart was dilated, but there was no evidence of any disturbance of the circulation in the intestinal veins.

The specimen consists of a piece of the descending colon and sigmoid, measuring 60 cm. in length. In its lower half are counted fourteen diverticula, many of which are filled with fecal concretions. The average diameter of the opening into a diverticulum is 0.5 cm. The average length is 1 cm., and the fundus of the sac is usually about twice the diameter of the neck. Each diverticulum has its os lying in a plane midway

between a lateral tenia and the mesenteric line, and the sac extends outward into an appendix epiploica. There is no gross evidence of any inflammatory thickening about the diverticula or in the intestinal wall adjacent to them. On the contrary, in those diverticula which are distended with feces, the fundus of the sac seems distinctly thinner than the rest of the gut wall.

Microscopically, transverse and longitudinal sections through the diverticula show no inflammatory changes. The mucosa is slightly flattened. The circular layer of muscularis becomes greatly thinned at the neck of the diverticulum, and soon disappears. A slender band of longitudinal fibers, containing considerable fibrous tissue, completely encircles the sac. The transverse section shows a large artery and vein in the subserosa of the fundus. The serosa is normal.

Case X.—This specimen was obtained at the autopsy of a male, 56 years of age, who died in the Bellevue Hospital of acute lobar pneumonia. The clinical history gave no evidence of any intestinal lesion. Neither the clinical history nor the autopsy gave evidence that any chronic disturbance in the intestinal venous circulation had been present.

The specimen consists of a portion of the ileum. At one point opposite the mesenteric attachment there is a Meckel's diverticulum, measuring 9 cm. in length and 3 cm. in diameter throughout its length. On this diverticulum are distinctly seen four secondary diverticula, each about 1 cm. in diameter and 0.5 cm. in depth. There is a slight constriction near the middle of the large diverticulum corresponding to the line of the obliterated vessel coming from the mesenteric border. On opening the intestine this pouch communicates with the lumen of the gut by a circular opening 2 cm. in diameter. The secondary diverticula can be seen opening into the large pouch.

Case XI.—A male, 66 years of age, died in the Bellevue Hospital from general arterial sclerosis and cardiovascular disease. General anasarca was present and there was very severe congestion of all the abdominal viscera.

The specimen consists of the cecum and a portion of colon measuring 12 cm. in length. Five diverticula are present, varying from 0.25 cm. to 2 cm. in diameter. The larger ones are filled with hard fecal masses (Fig. 5). The communication with the lumen of the gut is always smaller than the pouch of the diverticulum, but there is no neck. The expanded pouch around the mouth of the sac is thinned, and the wall of the pouch itself is distinctly thinner than the surrounding intestinal wall. The diverticula lie in planes between the mesenteric line and the lateral tenia on either side. One diverticulum is in the cecal pouch itself, and on the external surface lies 2 cm. external to the origin of the appendix vermiformis.

Microscopically, a section taken transversely through one of the diverticula shows the following: The sac is connected with the lumen of the intestine by a very small opening. The mucosa is reflected over the margin of this opening and lines the entire sac. The portion in the sac, however, is thinner than that lining the adjacent gut and is covered with a layer of structureless material. The submucosa is normal. The circular layer of the muscularis surrounds the sac, but shows a marked thinning, and more or less replacement with fibrous tissue. The longitudinal fibers are not found in the wall of the sac. A large artery and vein lie in the subserosa of the fundus of the sac. The serosa and subserosa are normal. The intestine adjacent to the diverticulum is normal.

Case XII.—The specimen was obtained from a male patient, 68 years of age, who died in the Presbyterian Hospital from carcinoma of the prostate, bladder, and liver, the primary lesion being in the liver. There was no evidence at autopsy of any interference with the circulation in the intestinal veins.

The specimen consists of the whole large intestine. In the cecum there are three diverticula measuring 3 to 9 mm. in diameter. Surrounding them is a distinct area of inflammation. The transverse colon and sigmoid show an increasing number of diverticula, all small in size. The diverticula are distributed irregularly and show no definite relation to the mesentery or tenia. These diverticula vary in diameter from a few mm. to 1 cm. The entrance to the diverticulum is always much smaller than the lumen of the pouch itself. The wall of the descending colon and the sigmoid is much thickened by tissue in the middle layers of the wall. At one point this thickening is extreme, the wall measuring nearly 2 cm. in thickness. In this situation the diverticula are very numerous, being closely packed together. Microscopically, a section taken transversely through two adjacent diverticula in the sigmoid shows the following changes: The mucosa in both sacs is intact but infiltrated with a large number of small, round cells of the lymphoid type. The submucosa shows a similar infiltration. Over the fundus of one saccule the submucosa is necrotic and contains several large vacuoles which suggest that the tissue has contained gas. As there are no polynuclear leukocytes about this area, it is probable that the change is a postmortem one. The

circular layer of muscularis has undergone considerable hypertrophy, a change which can be observed not only in the wall of the intestine between the diverticula, but in the lateral walls of the diverticula themselves. Over the fundi, however, the muscularis becomes thin. The longitudinal layer of the muscularis is not made out. At

Figure 9.—Diverticula of the colon, showing the openings of the diverticula into the gut. (Case XV.)

many points the muscularis of the sac wall is densely infiltrated with lymphoid cells. Large vessels occur in the subserosa of both saccules. The subserosa contains a good deal of adipose tissue and many lymphoid cells. The serosa is normal. Another section taken through one of the diverticula in the ascending colon shows no inflammatory changes, and no hypertrophy of the muscularis. A thin strip of the circular layer of muscularis surrounds the saccule.

Case XIII.—The specimen (museum specimen, Bellevue Hospital) consists of a portion of small intestine, 30 cm. in length. Seven small oval diverticula, varying in size from 0.5 to 1.5 cm. in diameter, occur along the mesenteric border between the folds of the mesentery, but bulging more on one side than on the other. In each case a vein may be seen travelling from the convex border of the intestine in the subserosa, and passing directly over the diverticulum to reach the mesentery. This vein is always present only on the side toward which the diverticulum bulges. The leaves of the mesentery can be stripped off the diverticula.

On opening the gut the communication between its lumen and the diverticulum is seen in each case to be smaller than the diameter of the diverticulum itself. Three additional openings are found communicating with diverticula too small to be identified from the external surface. The opening into the diverticulum is situated, in most cases, on one side of the mesenteric line. A few seem to correspond exactly to its line of attachment. The same relation of the diverticulum to the vein is manifest, and it is the course of this vein toward the mesentery that determines the direction of the growth of the diverticulum.

Microscopically, sections have been taken transversely through the gut at the site of one of the small diverticula. The mucosa and submucosa are everywhere normal. The muscularis extends down for some distance over the saccule, but is absent over the fundus. The longitudinal layer extends further down than the circular. It be-

Figure 10.—Microscopic section through a diverticulum. The muscularis terminates suddenly at the neck of the sac. The mucosa and serosa are greatly thinned. (Case XVII.)

comes gradually thinner and finally disappears. The serosa and subserosa are not thickened. There are no large vessels in the wall of the saccule. The intestine adjacent to the diverticulum is normal.

Case XIV.—The specimen (museum specimen, Bellevue Hospital) consists of a piece of small intestine 40 cm. in length, showing thirteen diverticula, varying in diameter from 0.25 cm. to 6 cm.; eleven of these are crowded together into a piece of intestine only 22 cm. long, so that there is practically no part of the mesenteric border free from a diverticulum. The same relationship between the diverticula and the mesentery and veins is present as described in Case XIII. The walls of the larger diverticula are somewhat thicker than those of the smaller ones. There is no communication between the individual diverticula even where they are close together.

Microscopically, a section taken longitudinally through the gut displays a portion of diverticulum of rather large size. The mucosa is flattened. The submucosa is normal. The two coats of the muscularis extend down over the saccule, but become much thinner at the neck. The circular layer becomes rapidly thinner and soon entirely disappears. The longitudinal layer appears to continue as a thin strip clear around the sac. The serosa and subserosa are normal.

Case XV.—The specimen (museum specimen, Bellevue Medical College) consists of several small pieces of colon showing diverticula packed rather closely together and varying in size from 1 cm. to 3 cm. in diameter (Fig. 9). They show the same general characteristics as the other specimens, but owing to the way in which the specimen has been mounted, the relation of the diverticula to the mesentery and vessels cannot be determined.

Microscopically, sections taken transversely through a small diverticulum show considerable postmortem change, but the different coats can still be made out. The mucosa and submucosa are normal. The muscularis, both the circular and longitudinal, extends up for some distance on either side of the neck, but becomes progressively thinner and soon disappears. Occasional bundles of the longitudinal fibers occur over

Figure 11.—Microscopic section through a diverticulum, showing the artery and vein in the wall of the sac. (Case XVIII.)

the fundus. The serosa and subserosa are normal. No large vessels are found in the subserosa.

Case XVI.—The specimen (museum specimen, Presbyterian Hospital) consists of the duodenum, which shows the presence of eight small diverticula, the largest measuring 1.5 cm. in diameter, all of which occur in close relation to the mesenteric attachment. All but one are situated in the portion of duodenum distal to the papilla of Vater. The general appearance and gross structure is the same as that described for those in other parts of the small intestine.

Microscopically, the diverticula were studied in transverse and longitudinal sections. The walls of the saccules are composed of normal mucosa and considerably thickened serosa. Both the transverse and longitudinal portions of the muscularis

come to a rather abrupt ending at either side of the neck of the sac. There is a large artery in the subserosa of one of the saccules. The intestine adjacent to the diverticula shows no change.

Case XVII.—The specimen (museum specimen, Bellevue Medical College) consists of a section of colon 10 cm. in length. On the two lateral aspects of the intestine are closely crowded together fusiform diverticula, from 1 cm. to 1.5 cm. in length and 0.75 in diameter (Fig. 4). The bases of the diverticula lie in two lines directly posterior to either lateral ternia. There is a distinct interval of normal intestinal wall lying between the mesenteric attachment and the diverticula on either side.

On opening the intestine, each diverticulum is seen to communicate with the lumen by an opening somewhat smaller than the diverticulum itself. This inequality, however, is not nearly so marked as in some of the other specimens. In two instances, two diverticula communicate with the intestine by a common opening, the septum which originally separated them having in part disappeared. In each of these cases the two individual diverticula lie in an oblique, nearly transverse plane.

Microscopically transverse and longitudinal sections through the diverticula present similar pictures. At one point the wall of the gut is greatly thinned out, and takes the form of a small saccule. The muscularis terminates suddenly on either side of the diverticulum, so that the wall of that structure is composed only of mucosa and serosa (Fig. 10). The former is very thin, and atrophic looking, the crypts having largely disappeared. The serosa is also quite thin. The intestine adjacent to the diverticula exhibits no changes. In neither the transverse nor the longitudinal sections can any large vessels be found.

Case XVIII.—The specimen (museum specimen, Presbyterian Hospital) consists of a piece of small intestine, measuring 135 cm. in length. Thirty-three diverticula are present. They are all in close relation to the mesenteric border in their origin and pouch on either side beneath the mesenteric leaf (Fig. 1).

In nearly every case a large vein, and sometimes an artery, may be seen coursing over the pouch of the diverticulum. The intestine has been preserved unopened, so that no description of the diverticula from the inside is given. They measure from 0.25 cm. to 6 cm. in diameter, all being of a globular shape.

Microscopically, a transverse section through one of the diverticula shows a small saccule opening into the gut through a narrow opening. The wall of the sac is composed chiefly of the inner and outer coats of the gut, the longitudinal fibers of the muscularis extending down for only a short distance on either side as a thin strip. The mucosa and submucosa show no changes. The cross-sections of two large vessels—a vein and an artery—occur in the subserosa of fundus (Fig. 11). The serosa shows no perceptible thickening. A longitudinal section through another diverticulum presents a very similar appearance. The muscularis, however, in this case, stops abruptly on either side of the neck of the saccule. A large vein is found in the subserosa. The intestine adjacent to the diverticulum in both cases appears normal.

Summary of Reported Cases—Four patients showed symptoms for which they underwent operation. Of these, three suffered from chronic symptoms, and were cured by operation; one suffered from acute obstruction; and was cured by operation. Eight specimens were obtained from autopsies on persons dead from causes not connected with the diverticula, and in none of them had any symptoms relative to this condition ever been present. The remaining six specimens were found in the museums, and no clinical or postmortem data were obtainable.

Sex—Of thirteen cases in which the sex is given, ten were female and three were male.

Age—The two youngest cases were 6 and 7 years of age, respectively. Three were under 30 years of age, and six were over 50. The ages of those giving clinical symptoms were between 22 and 43, thus demonstrating that neither the diverticulum nor its inflammation is solely a disease of advanced life.

The number of diverticula in each case was as follows: The least was one and the most was thirty-three, with an average of about ten. Location: Of the eighteen cases, seven involved the descending colon, or the sigmoid, or both; three involved the ascending colon; one involved the cecum; two involved the transverse colon; two involved the "colon," the particular portion not being given; four involved the small intestine, one of which was in the duodenum; one involved the wall of a Meckel's diverticulum. In five out of the eighteen cases, the diverticula occurred in the small intestine. In all but one of these the diverticula were in close relation with the mesenteric line. None of those in the large intestine was so placed, the greatest number, eight cases, being found between a lateral tenia and the mesentery. Only one was found in the convex border of the intestine. In three of the five cases occurring in the small gut, there appeared to be a definite relationship between the diverticula

and the mesenteric veins. No such connection could be established in any of the cases occurring in the large gut. In only one was there any evidence that a venous congestion in the inferior mesenteric veins had been present during life, while in eleven this was absent. This is in direct opposition to the findings of Graser. In the remaining six no information on this point was obtainable.

Of the fifteen cases from which microscopic sections were cut, twelve showed more or less muscularis about the particular sac studied. In the other three cases, the fundus of the sac was composed of only the inner and outer coats of the gut, the muscularis terminating abruptly at the neck of the sac. In five of the twelve cases on which a muscularis was demonstrated, both muscular layers were present. In five others, only the longitudinal coat survived. In the remaining two cases, only the circular coat could be demonstrated. By means of the Van Gieson's stain, traces of atrophied muscularis were found in several instances in which it had been overlooked in hematoxylin-eosin preparations. As a rule we have found that the larger the diverticulum, the thinner and more atrophied is the muscularis. The circular layer is generally the first to disappear.

Conclusions.

1. Diverticulum of the intestine is a common condition.
2. The large bowel is the most frequent site, particularly the descending colon and the sigmoid.
3. Children and young adults are subject to diverticula, and to the secondary changes occurring in them.
4. All diverticula are probably true in their incipiency. The false characteristics are the results of their growth.
5. An inherent weakness existing in the muscularis is probably an important factor in the etiology of diverticula. In the small intestine this weakness appears to exist along the mesenteric attachment.
6. Diverticula undergo the same pathological changes as the appendix vermiformis, and give rise to much the same general symptoms. These pathological changes are not uncommon.

We wish to express our thanks to Dr. Opie for the material from the museum of the Presbyterian Hospital; to Dr. Norris and Dr. Pappenheimer, for specimens from the Bellevue Hospital Laboratory: to Dr. Crowell, for specimens from the museum of the University and Bellevue Medical School; and to Dr. Moschowitz, for permission to include his interesting case in our series. We are also indebted to Drs. Leaming. Jachs, Agnew, and G. M. Smith, for photographs of the specimens.

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27. In the microscopic study of the diverticula, the following technique was used: The sections were cut either longitudinally—that is, parallel to the long axis of the intestine —or transverse to this axis, or both. All sections thus include normal intestine adjacent to the diverticulum and the structures occurring in the neck and fundus of the sac. The sections were stained with hematoxylin and eosin. In addition, duplicates of each section were stained by the Van Gieson method. In every instance, small diverticula, never over 1.5 cm. in diameter, have been used for the microscopical sections.
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DISTORTION OF THE MESENTERY AND ITS RELATION TO INTESTINAL OBSTRUCTION.*

By Joseph D. Bryant, M.D., LL.D.,

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For the purposes of this occasion, Distortion of the Mesentery is considered to mean the twisting or otherwise forcing out of shape of the mesentery by disease process, and thereby so disarranging its normal relation with the attached intestine as to change the orderly course of the latter with reference to it. Torsion of the mesentery, as commonly expressed, is not included in this title. It seems not at all unreasonable to conceive that the forcing out of shape in this manner of the mesenteric curtain, to the lower border of which the intestine is attached, would change the normal relations existing between them to a sufficient degree as to modify correspondingly the functions of the included intestine.

The stimulus prompting the conception of the title and promoting the birth of this paper, had its origin in the strikingly interesting, and to me, instructive features incident to a case recently coming under my notice from lay sources, which was characterized by long-standing and progressively increasing symptoms indicative of intestinal obstruction. The nature of the obstructing cause was at first problematical, being regarded as functional; then, as functional with organic complications, the latter of which finally dominated the varying picture of distress so long as the patient remained under observation. It, therefore, naturally follows that the syndrome of this case is divided into two parts, viz.: the early or the recounted part, and the later or the observed part, at least so far as the writer is concerned. And, in expressing the indications of disorder in this instance, especially those manifestations will be told which are regarded as not being inconsistent with a belief in the peculiar nature of the obstruction, and its probable location. A plan like this necessarily eliminates, except for comparison, many of the multitude of common symptoms of intestinal obstruction, and correspondingly abbreviates and emphasizes the text and the facts that are regarded as being expressly related to the problem.

It appeared, in this instance, according to the recounted symptoms, that, at longer or shorter intervals of time for several years, there had occurred brief attacks of intestinal colic usually accompanied with nausea and vomiting, as the distinguishing traits. The frequency and severity of the attacks, though differing in degree from time to time, gradually increased in these respects, until the uncertainty of the time of their coming and going, and of their severity, obviously founded a most unhappy and insecure state of affairs. Usually, in these instances, however, a mild anodyne, supplemented with a gentle cathartic, afforded prompt relief—a relief commonly marked by copious evacuations of semi-solid material, sometimes with distinctive features of indigestion, but with no evidence of obstruction. Afterward, however, a decided change occurred in this, the negative feature of the case. For, in an attack apparently induced, as often before, by indiscretion in diet, it is recounted that there developed after twenty-four hours, genuine symptoms of intestinal obstruction, which refused obedience for forty-eight hours longer to the usual remedial means employed in these instances. Soon after, however, a copious bowel evacuation succeeded an escape of offensive flatus, the apparent sequel of a deferred, hopefully employed, high enema. Complete comfort followed at once. But, singularly enough within an hour after the stool, nausea ensued which was promptly and finally relieved by abundant vomit having a distinct fecal odor. Also, it is told that during the height of this attack, the turpentine and the asafœtida separately employed in the high enemata for the purpose of fecal dislodgment were tasted by the patient soon after their introduction. A fact which happened thereafter, it is said, on two occasions with the use of asafœtida with a similar intention. After the prompt subsidence of this attack, I was told that comparative quiet reigned in the abdominal affairs of the patient for nearly eighteen months. Before, during, and subsequent, to this attack, nothing of diagnostic significance related to the affliction, could be ascertained by physical examination so long as the patient came under our notice. Later, the painful digestive attacks increased in frequency, happening once in four or five weeks, in fact, were not infrequently prompt complications of slight constipation and of errors in diet. And, too, before final relief from an attack came in sight, fecal vomit in varying amounts was in evidence—at

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least, once in three or four months. And, at one time, the attacks bid fair to wear the patient out through the torment of spirit and physique, which they imposed at uncertain intervals.

The pain was rarely severe, it being often readily controlled by a small amount (⅛ or 1-10 grain and less) of morphia, given hypodermically once in six or eight hours. The pain was located primarily, and throughout the attack, in the navel region. It sometimes came suddenly without premonition; again with a sense of indefinite gastric or abdominal distress; and often in a gradual manner, with or without important manifestations. Some general tenderness of the abdomen was present, especially if the attack was severe, but no circumscribed points of tenderness could be determined in slight or severe attacks until late in the history of the case, when, after severe attacks, varying and vague points of tenderness were noted only in the navel region. The region of the appendix and of the gall-bladder, however, was free from all uncomfortable manifestations. Local or general tension of the abdominal muscles was never observed. Tympany was absent during slight attacks, and was not pronounced during the severe. The pulse exhibited but little change from normal, except during the later part of my observation, when it, very naturally, was accelerated by pain and fever. The temperature (rectal) rarely reached 100 F. until during the later attacks, when it would go up a degree or two, and even higher, and then suddenly fall a degree or more in a few hours (6 or 8) before the symptoms of obstruction were relieved, usually by copious alvine dejections. So constant was this phenomenon in these later attacks as to become of special significance as indicating approaching relief. During the last two attacks known to me, the remission was quickly followed by abdominal pain, and return of temperature which, soon after, resumed the usual low figure of the preceding attacks. It would seem as if in these special instances, brief arrest of recovery had happened, resulting, perhaps, in slight re-obstruction and consequent increased degree of infection. Especially so, since their temperature of 103 F. and 104 F. for a short time, would then suddenly fall to nearly normal attended with perspiration. Nausea was common with the onset of the pain, and often vomiting, the vomit being composed usually of the contents of the stomach, followed by bile. In several instances, however, the vomit became fecal, sometimes very promptly and unexpectedly, and once primarily, then again, later in the course of the attacks. In one instance, free fecal vomiting, and a simultaneous large stool terminated at once a seventy-hour period of apparent obstruction. In this instance, the physical characteristics of the two discharges, oral and anal, were similar in color, odor, and consistency. The color was brown, the odor fecal, and the consistency semifluid. A chemical examination of these discharges disclosed the presence of indol and skatol in each, and with but little more of these agents in the stool than in the vomit—a difference which, at the time, might well have prompted the thought that the intestinal obstruction, in this instance, divided somewhat equally the field of abnormal development of these substances. For, were the obstruction located at the proximal side of the region of development, one would not expect the presence of either substance in the vomit.

In the majority of attacks, the symptoms of intestinal obstruction yielded quite promptly to high enemata and colonic irrigation. At times, however, these agents produced no apparent effect, even on repeated employment. It sometimes would seem as if the obstruction—at uncertain periods (30 to 75 hours after attack)—would yield more to intestinal effort than to human contributing influences. That is to say, the morbid physiology of the intestine itself apparently was more potent for relief on these occasions than were the special efforts of those in charge of the case. In one instance, however, when other measures afforded no relief, two quarts of warm sweet oil, slowly introduced as high as possible into the bowel, were, in the course of an hour, followed by copious discharges of soft fecal content, succeeded by prompt relief lasting for a brief period. A curious sequel to this experience was the frequent passage in the stools for about twenty-four hours, of varying small amounts of sweet oil. It appeared as if the oil had been sequestered in the bowel, so as to be returned in divided portions from time to time, as the actions of the bowel would require. Also a manifestation which pointed to the presence of isolated collections of fecal matter in the small intestine, happened in two instances later in the history of the case in the following way: The administration of a saline cathartic was followed promptly only by brown watery evacuations strongly impregnated with indol and skatol. This result would not be expected in the instance of an empty colon already rinsed well by saline catharsis and irrigation. In these instances, however, a liberal dose of castor oil was promptly followed by a large soft fecal evacuation. It therefore appeared as if the fluid dejections had passed across or through disseminated accumulated fæces in the small intestine, thus staining and impregnating them with indol and skatol. For, had the amount of fecal gathering disclosed by the cathartic been circumscribed in the

small intestine, there is no doubt that tumor would have been present on manipulation, hence the belief in circumscribed dissemination. In the second instance, after ingestion of milk the rapid appearance per anum of milk-colored discharges followed by an abundant fecal movement from castor oil, suggested the presence of fecal accumulation in the small intestine, especially when the colonic irrigating fluids, just before employed, had been returned uncolored. Again on frequent occasions, test doses of two grains of bismuth by mouth, in the instance of fluid diarrhœa, promptly discolored the anal discharges, thus clearly demonstrating the fact of incomplete obstruction and the absence of a special diarrhœa from below. And, too, following this, the normal fecal discharges returned without the help of remedial agents, suggesting the further idea that but little, indeed, of the fluid discharge could have come from a local intestinal irritation caused by a fecal accumulation.

It is but fair to say at this time that careful observation and study of the phenomena noted in this case, convinced the writer that, for some reason, an S trap-like arrangement in the course of the small intestine was present, and likely, too, in plural number, at the lower curves of which passing fecal matters accumulated sufficiently on different occasions to cause more or less, and sometimes complete obstruction, often accelerated by indigestible matters of sufficient amount or suitable size, to completely and suddenly occlude the remaining part of the lumen. More often, however, it was believed that the pockets were emptied by local intestinal muscular contraction with more or less pain attendant thereon, and, at other times, wholly, or in part by the aid of cathartics, more especially castor oil. As already intimated, it was believed that at times an incomplete occlusion was present, leaving only sufficient space to permit of the passage of saline evacuations over the fecal accumulations in the dependent parts of the receptive loops of the deformed intestine, thus tincturing the passing fluid with indol and skatol. The prompt passage, at times, of undigested milk and of bismuth-stained fluids for test purposes also served to substantiate the belief in incomplete obstruction. And, too, on careful thought no other form of intestinal obstruction appeared so well to meet the syndrome of this case. It was not improbable that this obstruction was located in the ileum not far from the cæcus, and also that the ileocæcal valve at times was pervious to fluids from below, and that active reverse peristalsis was a prominent feature.

It should not be amiss now to further interpret, so far as practicable, the other various phenomena which pointed toward and added interest to the pathologic picture just sketched.

The tasting on different occasions of the turpentine and asafœtida employed in high enemata for the purpose of overcoming intestinal obstruction, suggests at once that the obstruction could not have been complete, though so regarded at the time. Also, that reverse peristalsis had been rapid and pronounced at the time, as taste of the drugs happened during the brief retention of the enema. And, besides, for some reason, the ileocæcal valve was not on guard in a manner commonly supposed to characterize its office. In this connection, however, it is proper to say that intestinal peristalsis is not as simple a mechanism as is commonly supposed, and that antiperistalsis especially is a phenomenon the intricate nature of which is, as yet, not entirely settled.

Practically, however, antiperistalsis is reported as having carried nourishing and medicated agents from the rectum to the mouth in a brief time in many instances. The writer in 1892, in a hysterical patient, observed the vomiting from a test glycerine and methyline violet enema twenty seconds after its introduction into the bowel. A suspected communication in this case between the colon and the stomach was disproved by explorative examination. About the same time, the attachment of the divided ileum to the sigmoid flexure was practiced by the writer in order to short-circuit the intestinal contents in the instance of an obstinate fecal fistula of the transverse colon. But, only a change in the consistency of the fecal discharge was observed, as the soft discharges of the ileum were carried up the descending colon by retrograde peristalsis, and escaped as before from the cutaneous opening of the fistula. Also, as a matter of established fact, and apparently shown by this case, a continuous peristalsis going rapidly from the rectum to the stomach, and, another kind arising at an irritated part of the intestine, and going from it in opposite directions may take place.

That the inhibitory influence of the ileocæcal valve on peristaltic intercourse of the large and small intestines cannot be regarded as definite, is evidenced by the report that in 60 per cent. of subjects (Debierre) the valve is found to be permeable from below.

It seems permissible now, to point again and more fully to symptomatic features of the case which had been regarded as being of special significance in connection with the peculiar form of obstruction to which they had been assigned. Among them may be classed the nearly equal amounts of skatol and indol contained in the fecal mat-

ters simultaneously discharged from the mouth and anus. Of course, I was aware of the flood of fallacies that beset this proposition, but, it came to my mind and was not dismissed. The normal habitat of these diagnostic products of fecal substance is peculiar to the cæcum and the first part of the colon. And, in this instance, it appears that the ileocæcal valve was pervious from the colonic side. Therefore, at first sight, it could be easily said that primarily both oral and anal dejections were largely the product of cæcal and colonic activities, whose respective exits were made possible by the presence of an obliging ileocæcal valve. But, if such had been the case, the amount of skatol and indol in the oral dejection might well have exceeded that of the anal, since, to the contents of the cæcum and nearby colon are these products easily peculiar. But inasmuch as the processes of decomposition breed skatol and indol anywhere in the intestine, in amounts proportionate to the contributing influences, and, as in this instance, the putrefaction changes were general throughout, and, also, that an incomplete hindering obstruction of some sort was lying between the cæcum and the stomach, it was not singular, and one would expect the greater amount of these products to favor the anal exit of the area of their natural production. Also, classed as indicating the possible location and probable mechanism of the obstruction, will be recalled certain facts already stated in the early history of the case, viz.: The slow development, too slow, in fact, for the progress of the common kinds of intestinal obstruction. And the associated indications conform therewith. The phenomena recounted regarding the high sweet oil enema; the colonic irrigations; the skatol and indol impregnations; the milk and bismuth exhibitions; the castor oil responses; the forecasting indications of spontaneous relief, etc., etc., appealed to the author with sufficient force to put in mind the theory already expressed, *i.e.*, "an S trap-like arrangement of probably multiple parts in the course of the small intestine." This theory was promulgated before a tangible opportunity was afforded to determine the seat and mechanism of the obstruction by means of material examination. Finally, however, by so doing, it was determined that nothing physically appreciable was at fault with the colon, the cæcum, or the appendix. The first four or five inches of the ileum were normal. The succeeding seven or eight inches and the mesentery connected therewith were abnormal, the latter being distorted by chronic inflammatory process, so as to cause scalloped irregularities of the attached intestine for a corresponding distance. The wall of the intestine at this situation was much hypertrophied, thus giving rise to marked encroachment on the lumen of the gut, which otherwise was enhanced in places by the acute angles of the scallops themselves. The intestine proximate to the obstructed part was moderately dilated and hypertrophied for a considerable distance.

The marked hypertrophy which characterized the disordered part of the intestine is regarded as the natural product of its crippled condition, especially in view of the well-known fact that the interference with the normal flow of a fluid through its natural channel at once provokes functional resentment of a greater or lesser degree on the part of the motor forces interested with the conduct and care of the function. And, also, that the effort required to keep pace with the demands of increasing interference develops the compelling forces correspondingly, as is made manifest by the increasing growth of the responsible parts engaged in the duty of functional activity and preservation. We can quite easily understand how, as in this instance, that near-together consecutively arranged developing interferences (scallops) with intestinal function could, sooner or later, cause slight, temporary, and finally more or less decided obstruction to the flow of the intestinal contents, attended with corresponding increase in dimensions and power of the propelling force, as represented by the muscular development of the part thus directly involved.

It would appear to me that the disclosures of the examination have reasonably established the conjectural diagnosis as related to the location and the mechanism of the obstruction. Also, that the phenomena recounted in connection therewith fit the physical findings amply, certainly much better than they can be adjusted to the mechanism of a different form of intestinal obstruction.

A careful examination of the literature of intestinal obstruction as related to mesenteric distortion (not volvulus) by competent persons, reveals no instance of similar intestinal disfigurement, or of like clinical history. In one instance only it appeared that the pressure of a large tuberculous mesenteric gland on the veins of the mesentery of the ileum had produced œdematous thickening of the walls of the corresponding part of the intestine to a degree causing sufficient closure of the gut, and modification of its functions to produce acute intestinal obstruction, for which resection of the part was made.

What I have offered, on this occasion, is most respectfully submitted, and, for the time being is all I would care to say regarding a matter which only time and multiplied opportunities can fittingly adjust to the topic of intestinal obstruction.

THE EARLY DIAGNOSIS OF INTESTINAL CANCER.*

IRVING S. HAYNES, PH.B., M.D.

Frequency and Mortality—Cancerous disease is rapidly increasing. The mortality rate is more than double what it was forty years ago. Nearly 40,000 people die annually in the United States from cancer (Park). After the age of 35, one man out of seventeen and one woman out of nine will die from cancer (McGlinn).

Curability—There is no medical cure for the disease. There is no surgical cure except with certain varieties in accessible regions early in the disease and after wide excision. Even then the surgical cure is only about 25 per cent. for external cancers, very much less for those within the abdomen, and none at all for those arising within the thorax.

Surgeons, then, do not feel flattered by their record of cures in this disease.

Improvement in the mortality rate can come only in three ways. Wide excision, earlier operation, or by an anti-cancer serum. The first is now attained by experienced operators; bacteriologists are striving for the last, but so far without any certain results. Our only hope then, of lowering the mortality rate, is by an earlier diagnosis and operation.

Difficulty in Diagnosis—The early diagnosis of superficial cancers is often a difficult problem and many times definitely settled only by the microscope during or after the operation. Internal cancers are very much more difficult to recognize, and it is at times impossible to draw any conclusion beyond the fact that there is something serious the matter, its exact nature unknown to us, but which ought to be subjected to an ocular examination.

I am gradually growing into that frame of mind which makes it necessary in intestinal (and gastric) disturbances to *prove* that the condition is *not cancerous* than to leave this as the last alternative. It is wise then, I think, to suppose that cancer may be present and arrive at the true diagnosis by exclusion.

In order to keep within the time I shall limit this paper to a brief consideration of cancers of the small intestine below the duodenum and the large intestine above the rectum. Inasmuch as cancers of the small intestine bear a very small proportion, one to ten, to those in the large bowel, this paper virtually deals with cancer of the colon, with brief references to growths in the small intestine.

Carcinoma, Morbid Anatomy—Although there are a variety of malignant growths which may invade the small and large intestine, carcinoma occurs so much more frequently than all the others that it is a safe statement to make that tumors of the intestine are almost invariably carcinomata. They are not very malignant at first, grow slowly along the line of the blood and lymphatic vessels, that is circularly around the bowel, and with only a moderate tendency to invade the lymphatic nodes or be disseminated to other organs until late in their course. The cancer ring around the intestine is often very narrow, less than an inch in width, and not more than one-quarter of an inch in thickness.

Its obstructive symptoms are not due to a large mass of cancerous tissue, but to the constriction and finally total occlusion of the intestinal canal by the contraction of this narrow cancerous ring.

Symptoms—The symptoms of intestinal cancer may be considered under three heads or stages.

1. The pre-stenotic stage.
2. The stage of stenosis.
3. The stage of obstruction.

This classification is purely arbitrary. One stage merges into another, and all are only phases of the onward march of the disease to a fatal termination. Yet, a consideration of the symptoms under this classification is not without some advantage, for it may serve to fix our attention upon some few symptoms in the earlier history of the growth so that, when the next case comes to us, we may *suspect* the cause and secure an operation before the onset of terminal symptoms.

In all stages of the cancer the symptoms might be considered under two heads, those produced by and due to the growth per se, and those caused by its effects upon the function of the bowel.

The Pre-Stenotic Stage—In the pre-stenotic stage there are no symptoms due to the growth itself, these (pain, emaciation, tumor, cachexia) are only late manifesta-

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tions of the malignant process and, when present, indicate an absolutely hopeless condition. The effects upon the function of the bowel are slight, if any, so slight that, as a rule, the physician is not consulted. Practically we are at present powerless to make a diagnosis in this stage. We are groping in the dark. A faint glimmer is seen, and we hope it will grow into a light that will guide us to a sure diagnosis, in the recent discoveries of the hemolytic reactions of the blood in cancer. But the method is yet in the stage of investigation, and its execution and results too uncertain for our dependence.

The earliest symptoms we could expect would be those of intestinal indigestion. A very indefinite phrase, that covers anything from overeating to the early symptoms of cancer, or from gall-stones to chronic appendicitis. Be this as uncertain and indefinite as it is, we can yet hope that we may become sufficiently interested in such a case of intestinal indigestion proving rebellious to ordinary treatment to carefully consider the possibility of something serious as the etiological factor, and thus be on the lookout for the earlier symptoms of stenosis.

The Stenotic Stage—The earliest symptoms of this stage, those which attract the attention of the patient to himself, are indigestion, constipation, gas in the bowels and attacks of colic which gradually grow worse. Gas accumulates, there is a feeling of fullness and discomfort after eating, while nausea and vomiting will appear later. Constipation is the one significant symptom which must be carefully investigated. It is steadily progressive. Cathartics must be taken in increased doses to obtain any results. With this there is the growing frequency and severity of the attacks of colics. To avoid errors in diagnosis our examination must be methodical, careful, critical, exhaustive.

First, the history. This must be minute and complete. Second, the physical examination, inspection, palpation, percussion, auscultation, sigmoidoscopy are all systematically employed. Third, the examination of the stool.

The *macroscopical* examination takes in the color, consistency, form, food remnants, pathological constituents, as blood, pus, mucus, foreign bodies, concretions, gall-stones, etc., and parasites.

The *microscopical* examination covers, besides food remnants, blood, pus and mucus, the possibility of masses of cancer tissue. The chemical examination determines if there is occult blood present.

As the stenosis increases, the colicky attacks become more numerous and severe. The gas will be heard and may be felt in accessible portions of the abdomen passing through the constricted intestine.

As a result of the obstacle to the fecal current the segment of intestine above the constriction becomes hypertrophied. During the attempts of the bowel to empty itself, active peristalsis may be visible through thin abdominal walls, and the intestine may be felt as an elongated mass, the "intestinal stiffening" of Nothnagel. Diarrhœa may alternate with the constipation, because a catarrh of the intestine develops above the obstruction, the free secretion mixes with the feces, softens and liquefies them so that a looseness of the bowels results. After a few movements, however, the constipation is again present as bad as ever. The feces will be pencil or ribbon-shaped, or they may be in small lumps like sheep-dung. They may be foul smelling, and blood, pus and mucus may be present. This is not constant and still more rarely is cancerous tissue found in the movement in this or the last stage.

The degree of interference with the fecal current depends a good deal upon the location of the lesion. If in the small intestine, or in the beginning of the large, inasmuch as the contents of these portions of the bowel are fluid, constipation develops slower and later than when the growth is located lower down in the colon.

With the preceding symptoms a stenosis is present.

Where is it?

Without a tumor being present, and depending upon the symptoms and our means of examination, we may arrive at the probable location of the lesion in the following manner:

Rectal injections of plain water or normal salt solution will afford some clue. If a small quantity of the fluid is quickly expelled from the rectum, the lesion is probably in the upper part of the rectum, if several pints are injected without returning, the trouble is probably at or above the cæcum. With intermediate quantities retained, the lesion may be estimated to be somewhere between these two points, with the sigmoid as the favorite location.

Gas also may be injected into the rectum and the distension of the bowel followed by palpation and percussion to the cæcum. Its arrest signifies the probable location of the constriction.

The most valuable means we have at present for locating a stenosis in the colon is by the X-ray photograph of the large intestine after it has been injected with a bismuth emulsion. The plate will show that at the site of the stenosis the band or shadow cast by the bismuth is suddenly narrowed, broken or arrested.

The radiographs exhibited in connection with this paper were made by Dr. Lewis Gregory Cole, of New York, and were kindly loaned to the writer to illustrate the possibilities of radiographs of the large intestine after injections with the bismuth emulsion, and the assistance such photographs render in the localization and diagnosis of lesions of this portion of the intestinal tract.

Should the cancer be located at its most usual site, viz.: the lower end of the sigmoid, the narrowing in the lumen of the intestine may be seen through the sigmoidoscope, and its calibre ascertained by graduated olive-tipped bougies.

Palpation of the abdomen may disclose the "intestinal stiffening" and percussion show that the enlargement is a tympanic segment of the intestine.

What is it?

Bands and adhesions from previous operations are ruled out by inspection of the abdomen. Herniæ by examination of the various hernial rings. Tumors of the neighboring viscera, distended gall-bladder, ovarian cysts, fibroid tumors, pregnant uterus, the sausage-shaped tumor of an intussusception can be negatived by abdominal, rectal and vaginal examination.

A fecal mass, polypus, enterolith, gall-stones, or worms, form a tumor possibly palpable. Here the preceding history, onset and course of the disease and urinary and fecal findings will aid in correct diagnosis.

In reference to a fecal tumor it must be remembered that it may form above, and around a cancer, so as to mask the real growth. It may also present the hard, nodular contour of a carcinoma. However, it can be indented and compressed between the fingers, and it will not resume its previous shape.

The narrowings, which follow tubercular, syphilitic and fecal ulcers, will require careful examination. Tubercular ulcers are most common in the lower part of the ileum, where Peyer's patches are most numerous. The ulceration begins in the lymphoid tissue of these patches. Tuberculosis elsewhere or with a positive vaccination reaction and with tubercle bacilli found in the feces (which is rare); the history of an initial lesion or secondary symptoms; the history of chronic constipation with normal movements at times, in spite of the blood, pus, mucus, which will be present in these conditions, will assist to a correct opinion.

Other conditions, which need to be kept in mind, I will only mention a movable kidney, or tumor of the kidney, tumor of the pancreas, mesentery, a Riedel's lobe of the liver.

The one condition that will require careful consideration in the stage of stenosis is *chronic spastic constipation*. There is indigestion, gas is present, there is intestinal colic of varying frequency and severity, the large intestine may be palpable as a hard, contracted, tender tube, and the stools are hard, small calibre, and contain more or less mucus and blood. However, proper treatment and diet extending over a reasonable time will relieve the condition and normal movements be obtained with disappearance of the symptoms.

A chronic intussusception, which has existed for several weeks, and in which incomplete history is obtainable, as from many of the ignorant poor, will cause but slight trouble in diagnosis. The youth of the patient, the sausage-shaped tumor and bloody mucous stools with severe colic and tenesmus and possibly a tumor felt through the anus, will make the condition plain.

Operation in the stenotic stage promises fair results. The growth, as a rule, is limited to the gut and has not invaded the lymphatic nodes or other organs. The intestine above the stenosis is not much larger than that below it. The patient has not been poisoned by the cancer nor by the prolonged absorption of toxic intestinal products. He has not been greatly weakened by suffering and is not emaciated to any appreciable degree. He is, therefore, in a fit condition for the major operation of intestinal resection and anastomosis, with fair chances of a permanent result. If recurrence does take place, it is apt to be retroperitoneal or in some other organ, chiefly the liver, and the patient dies from the cancer and not from intestinal obstruction. He makes his exitus in comparative comfort and not in agonizing suffering.

The Stage of Obstruction—This is the last stage. The conditions are acute, and the indications imperative. The obstructed intestine must be relieved at the earliest possible moment. It is well to make as careful a diagnosis as possible, but *the search for the cause must not delay the relief of its effect*. While I shall attempt to consider the differential diagnosis, I do not intend thereby to advocate delay. Operate at once and

make your probable diagnosis while scrubbing up the patient if there has not been time for this before.

Symptoms—The stage of obstruction is usually abruptly ushered in. In a few hours the patient may be in collapse and practically moribund. At other times the condition progresses gradually from the preceding stage of stenosis to that of complete stasis of the fecal current.

Obstruction of the small intestine gives the most severe symptoms, the higher the lesion the more acute the effects. There is vomiting, early, persistent, rapidly becoming fecal. The distention of the intestines and stomach forms a prominence about and above the umbilicus. This distention may be relieved to some extent by the vomiting to rapidly reappear. The lower and lateral parts of the abdomen are retracted. The pain and prostration is severe. Rectal injections bring down large fecal movements, without in any way alleviating the condition of the patient. The urine is very scanty, and the indican element is greatly increased.

With obstruction in the colon the symptoms develop more slowly, and, while the termination is fatal when untreated, the progress towards it is by freight rather than by express train. The distention of the intestine gradually extends upward, reversing the course of the intestine. It appears first in the hypogastric region (with sigmoid obstruction), then the left flank, then across the upper part of the abdomen, next into the right flank, and finally expands the central portions of the abdomen as the small intestines become distended.

At the beginning of the attack, before the intestine is paralyzed by the over-distention, violent peristaltic movements may be seen in thin walled subjects. The intestine, just above the obstruction, will also present the stiffening of Nothnagel. Vomiting supervenes late and only at the last is it fecal. The urine is not appreciably affected and the indican element is not increased. Rectal injections produce no fecal results and even gas does not pass the bowel.

If the caecum is the region involved the clinical picture is more acute than this and less so than when the small intestine is the seat of the disease. The middle portions of the abdomen are distended first and the flanks are retracted and dull to percussion.

With complete obstruction anywhere in the canal the final picture is the same. The abdomen is distended to the limit, the diaphragm is elevated and the liver dullness lost. The urine diminished. There is fecal regurgitation, hippocratic visage, coma and death.

The Differential Diagnosis—Strangulated herniae are ruled out by examination of the hernial orifices.

Tumors in the pelvis are ruled out by examination of the rectum or vagina or both.

Volvulus is usually in the aged, is rare at any time, and is one of the least frequent causes of obstruction, and peritonitis supervenes early. It may follow obstruction from a cancer or fecal mass and be caused by the displacement of the tumor twisting the gut. The diagnosis of cancer in this event would be practically impossible unless there is a history of preceding stenosis.

With volvulas, kinks, twists there is a history of previous good health and sudden onset of the obstruction. Pain is a marked symptom, vomiting is late, with a low twist, but early with one high up. Early in the condition Wahl's sign is present, *i. e.*, the intestinal coil immediately above the site of the obstruction is "fixed, motionless and inflated." This is due to the fact that in this variety of obstruction the intestine immediately above the constriction is not hypertrophied, and it is speedily over-distended and becomes paralyzed, while, with an obstruction following a cancer, the hypertrophy of the bowel prevents over distention from paralysis until later. Neither for the same reason is there intestinal stiffening of Nothnagel.

Intussusception—This occurs in infants usually, the onset is sudden, with pain, tenesmus, bloody mucus stools. A sausage-shaped tumor may be felt in the abdomen and its end by a rectal examination. Only rarely will acute obstruction from cancer be confounded with acute pancreatitis, thrombosis of the superior mesenteric artery, or acute poisoning with collapse and vomiting. Colics with constipation, of hepatic, renal, or intestinal origin would be cleared up after a careful history and analysis of the clinical symptoms. Paralytic ileus follows some severe abdominal injury, infection or operation.

In obstruction from peritonitis there is not the preceding history of gradual stenosis with apparent good health, but a condition of preceding acute inflammation of the appendix, or acute gonorrheal inflammation in the woman, or possibly a pelvic peritonitis following abortion or child birth. A ruptured ulcer of the stomach, duodenum or gall bladder will give a history of onset and course with clinical symptoms unlike those of cancerous obstruction, and the diagnosis would not be in doubt except at the last stage and without a clear history. At all events, in all of these conditions, excepting

that of peritonitis following acute gonorrhœa in the woman, the indication is for immediate operation.

Some authorities state that the presence of a tumor is absolutely necessary for the sure diagnosis of cancer. This may be true. At the same time, in the cases upon which I have operated, the diagnosis was made of probable cancer before operation, no tumor was present on external examination, and none found until sought for at its usual location in the lower end of the sigmoid deep within the pelvic cavity. A tumor has even been missed entirely at operation for relief of complete obstruction from cancer, even with the hand of the surgeon in the abdominal cavity to be discovered later at a more leisurely performed operation.

To wait for the appearance of a tumor in chronic bowel troubles, when there are symptoms of stenosis which do not disappear after careful treatment for a reasonable time, is to miss the golden opportunity and invite the inevitable fatal result. Delay here more than anywhere else is fatal. As Ochsner says, all you really need to do is to decide that a laparotomy is necessary. The exact condition can be determined with certainty at the operation and the proper treatment instituted.

Operation in the Stage of Obstruction.

An operation at this stage is merely palliative, very rarely will it be curative. The aim is to furnish an outlet for the dammed-up fecal current, in the most favorable location and in the shortest time.

If the obstruction can be located in the lower end of the colon, an intermuscular, left-sided, colostomy is the operation of choice. If in doubt as to the situation of the lesion, open in the median line below the umbilicus. No radical measures should be attempted. Excision and anastomosis may be performed later if the patient survives. The only single indication is to open the bowel and give vent to its contents.

After either of the above incisions and the peritoneum has been opened, draw out the presenting intestine, on the left side it will usually be the sigmoid, in the middle line it may be the sigmoid also or the small intestine. If the sigmoid, look no further, if the small intestine and the obstruction is in the cæcum, attempt to get as near the obstruction as possible, without taking much time in the search. Intelligent haste is necessary in this instance. Quickly suture the intestine to the skin, tie in a single short Paul's tube and leave the rest to nature. If the patient lives, a radical operation can be done at a later time. To attempt a radical operation at this stage is to hasten the death of the patient. The patient is in extremis, the abdominal condition very bad. The intestines are greatly distended above the constriction, its walls are thin, friable and may be ulcerated. Anastomosis is difficult to accomplish and usually futile, for the patient usually dies. If he lives, it is with a fecal fistula, and a secondary operation is required in any event. Nothing has been gained over a simple preliminary and temporary colostomy, and the patient has been compelled to endure an unnecessary severe risk.

Summaries of Clinical Records of Cases of Intestinal Obstruction due to Various Causes.

Case I—*Post-Operative Obstruction*—A private patient was operated upon for double pus tubes. This was followed by intestinal obstruction and the abdomen was opened a second time. The small intestines and the cæcum and ascending colon were distended with gas, but the rest of the large intestine was collapsed. On drawing the ascending colon downward a kink at the hepatic flexure was straightened out, the intestinal contents began to pass through the collapsed intestine and the bowels operated through the natural passage while the patient was on the table. The obstruction seemed to be due to an exaggeration of the hepatic flexure, and, after the gas once began to accumulate in the ascending colon and distend this portion of the intestine, the obstruction became complete. There were no evidences of any inflammatory action at the site of the obstruction. The patient did not recover from the shock of the second operation

Case II—*Perforating Carcinoma of Splenic Flexure, General Diffuse Septic Peritonitis*—A man about 50, was brought into the hospital *in extremis* and without history. All the evidences of a diffused septic peritonitis were present. The abdomen was drained in the median line, the patient's condition precluded any search for the cause. Death followed in a few hours. Autopsy showed a sloughing carcinoma of the splenic flexure, which had perforated and caused the septic peritonitis.

Case III—*Carcinoma of Transverse Colon, Obstruction*—Private patient, man 55, called in the midst of obstruction of the bowels, with severe colics. No vomiting. Abdomen distended moderately. High enemas and small doses of salines relieved the obstruction, which was caused by fecal impaction, just above a constriction in the transverse colon. After the bowels were unloaded, the tumor could be felt and a typical

history of stenosis obtained. Operation was advised and performed by another surgeon. I was not asked to be present at the operation, but the doctor was thoughtful enough to leave a diagram of his findings. The cancer involved the pylorus and also the transvere colon, binding them together. A gastrectomy and gastroenterostomy, and an enteroenterostomy were performed on the stomach and colon respectively.

The patient survived five hours.

Case IV—*Intestinal Obstruction from Acute Gonorrhoeal Peritonitis*—A young girl, 18 years of age, seen in consultation. Gradually increasing obstruction, with symptoms of peritonitis in the lower part of the abdomen. Was such a refined girl, and, as she absolutely denied all sexual causes, I was misled and operated for a probable perforating appendicitis with pelvic peritonitis. I found an acute gonorrhoeal pelvic peritonitis. Later the girl admitted intercourse and gave a typical history, but unfortunately she died.

Case V—*Carcinoma of Caecum, Stenosis*—Man of 47, hospital case. Diagnosis was made of carcinoma of the cæcum, with mild symptoms of stenosis. Marked emaciation and cachexia. A radical operation was undertaken. The growth had telescoped the large intestine to the middle of the transverse colon. What would have ordinarily been about two feet of intestine, with the retroperitoneal glands and the adjacent peritoneum were removed. The intestine was implanted into the colon. Union was by first intention and the abdominal condition was all right, but the patient gradually failed and died in ten days.

Case VI—*Carcinoma of Sigmoid. Stenosis, Obstruction*—Private patient, woman about 60. Typical history of slowly developing stenosis in the lower part of the large intestine. Exploratory operation was urged but refused. The case was under my care for five months. After the third month a distinct, small, hard, freely movable tumor could be at times palpated in the lower abdominal region. It was supposed to be in the sigmoid. The patient followed the usual course of increasing malignant stenosis. Emaciation, cachexia and symptoms of obstruction supervened, and she died from exhaustion.

Case VII—*Apparent Obstruction of Bowels, Due to Renal Colic*—A large, fleshy man, 40 years of age. Seen in consultation. Apparently complete obstruction of bowels, from his own and the attending physician's history. Close questioning, careful examination of the patient, and working along the lines of exclusion the diagnosis was reached of renal colic, even without the presence of visible blood in the urine. The subsequent history of the case, with the passage of a small calculus, confirmed the diagnosis.

Case VIII—*Obstruction from Chronic Intussusception*—An Italian child, four years old, was brought to the hospital with a distended abdomen, severe colics, tenesmus, bloody-mucous stools with, and at times without, fecal matter. An elongated cylindrical tumor at the right of the umbilicus was easily felt. The condition had existed for about four weeks and had followed an acute attack of abdominal pain, colic, straining and bloody discharges from the anus. Diagnosis, chronic intussusception. Operation showed that the intussusception was at the ileo-cæcal valve, involved about six inches of the ileum, and was not gangrenous nor adherent, strange to say, although the bowel was thickened and stiffened by chronic edema and exudation. The intussusception was reduced without much difficulty. The child left the hospital in two weeks cured.

Case IX—*Total Obstruction from Carcinoma of Sigmoid*—W. K., male, age 55 years, tailor. Russia. Brought to Harlem Hospital by his son, Dr. Kahn, March 28. 1909. to whom I am indebted for the following account of his father's illness. Personal history. Was always healthy and strong. Appetite always good. Habits regular. Used alcohol, tea, coffee in great moderation. Has never been ill. Married at 23, all children and wife alive and healthy.

Present illness. Began *two years ago,* when the patient was suddenly seized with colicky pains over the entire abdomen. Felt nauseated and vomited several times during the attack. Bowels at this time were constipated but soon *diarrhoea* set in. Examination during the attack revealed no abdominal rigidity or tenderness and no mass could be felt. By administration of cathartics attack passed off in about thirty minutes. Patient resumed his usual occupation. This attack, and the following attacks, were attributed to some indiscretion in diet. For a day or two preceding this attack, as well as those which occurred later, the bowels were constipated. About three or four months later the patient was again seized with a similar attack, which disappeared under the same treatment. And so during the past two years, these attacks would come on suddenly, without any premonitory symptoms, except slight constipation at intervals of a month or two. Has had perhaps six or eight attacks. Towards the end the attacks became more frequent, but were not severe in character

nor longer in duration. At no time was there abdominal rigidity or tenderness, nor could a mass be felt, and, at no time, except during the last attack was the pain localized. The patient was examined by four different physicians during the various attacks, with negative findings.

Between the attacks the patient felt very well and was able to attend to his business. But for a month before the last seizure he complained of a *gnawing pain* in the left epigastric region and this pain would be eased by pressure. In the morning his wife noticed during the last month *blood stains* on the sheet. Feces were never examined chemically or microscopically, but *blood* was *never seen* in them. *Has not been growing weaker* nor *has he been losing weight.*

The fatal attack, like the preceding, came suddenly on March 27th, in the afternoon. The pain at this time was unusually severe, particularly over the entire left side of the abdomen. Vomited moderately, at first bile, but in the later part of the evening had one attack of feculent vomiting. Could retain nothing on his stomach *Constipation* during the attack *was absolute.* All remedies to provoke a bowel movement were futile. He claimed to have had a movement of the bowels the day before. During this attack he was examined by three physicians, with the usual negative findings. The pain and vomiting continued and soon his condition became very bad. He was then brought to Harlem Hospital, where I saw him for the first time, in company with his son, Dr. Robert Kahn.

History by the Writer.

The patient was *in extremis.* Pulse weak and rapid. Surface dusk and covered with a cold, clammy perspiration. Abdomen moderately distended, symmetrically. Tender all over and nothing localizing. No mass could be felt in any part. My diagnosis was carcinoma, probably of the colon. The son thought it was a case of volvulus, because of the severity of the present attack and for the reason that his father had not lost flesh nor strength, and he had been able to keep the bowels open with small doses of cascara. I operated at once. The abdomen was quickly opened below the umbilicus, the distended sigmoid immediately ballooned through the wound. No time was lost in exploration, but the hand, passed into the pelvis along the distended sigmoid, felt a small, hard mass deep in the rectovesical pouch. This was brought into the lower angle of the wound and tacked there by a couple of sutures. The intestine above was opened and a large half-inch drainage tube passed into it and fastened there by a purse-string suture. The bowel was also sutured to the skin by a few catgut strands and the region well protected by a strip of iodoform gauze. Fluid feces and gas began to run off at once. I wish to emphasize the fact that, with this man at death's door in the final stage of carcinoma of the colon, there was no emaciation, no cachexia, no tumor palpable from the outside. He also had a subcutaneous layer of fat, the extraperitoneal fat was unusually thick, the intestines and mesentery were just loaded with it, as were also the appendices epiploicæ. The growth itself did not extend beyond the calibre of the intestine. In other words, with the intestine normally distended, no tumor would be apparent. This growth had caused total obstruction, yet it had produced no external bulging, was not more than one-half inch wide and looked exactly as if a string had been tied around the intestine closely enough to constrict it, and that the sides of the intestine adjacent to the ligature had become adherent. But for the hardness of the growth, its presence would not be surmised by merely looking at the outside, because the intestine was so covered with the fatty tissue. The growth was not adherent to any other structure. I did not spend any time in investigation but, from my brief examination, no enlarged lymphatic nodes were felt in the mesentery. I cannot say they were not affected, however. Had this case been diagnosed and operated upon any time previous to this last attack his chances of recovery from the operation would have been excellent, and the chances of a secondary recurrence at the minimum. No attempt to excise the growth was made. The patient lived six and one-half hours.

Case X—*Perforating Ulcer of the Duodenum with Extensive Adhesions. Diagnosed as Carcinoma of the Colon*—January 12, 1909. Man 35, admitted to the hospital for the radical cure of right inguinal hernia. Besides this he gave a history of digestive disturbances extending over some months, but without any localizing features. There was a small insensitive mass at the right of the umbilicus and a little above the site of McBurney's point. From the history and the mass I looked upon this condition as a possible carcinoma of the cæcum or appendix. After finishing the Bassini operation another incision was made over the tumor through the right rectus muscle. The mass was then seen to involve the ascending colon, hepatic flexure, beginning of the transverse colon and the duodenum and adjacent pyloric end of the stomach. The gall bladder was free. From its clinical appearance I looked upon the mass as an

inoperable carcinoma and closed the abdomen. For want of something else to do the patient was placed upon large doses of potassium iodide. His wounds healed by primary union and he left the hospital. His family physician, Dr. Muller, then kept him under observation. Last May the patient reported to me. He was in perfect health. Both scars and wounds had healed firmly and remained so and looked finely. My surprise was increased when, upon examination of the abdomen, I could find not the slightest trace of the growth which had looked so ugly at the operation. I then sat down with the patient and got a very careful history, which had not been obtained by the internes. This history, with the subsequent course of the disease, lead me to believe that the original lesion had been an ulcer of the duodenum, which had perforated gradually, allowing time for the adhesions to mat the intestines about it firmly together. I saw this state of affairs, when at the extreme of adhesion and exudation and, from its close resemblance to a malignant growth, thought it was a carcinoma. The potassium iodide, rest, diet and time had perfected a cure and promoted absorption of the excess of exudate. This again demonstrates the importance of obtaining a full preliminary history.

Case XI—*Carcinoma of the Lower End of the Sigmoid. Stenosis*—A. W., 44. Entered Harlem Hospital April 13, 1909. Printer. Habits good. Smoked a pipe all day. Has had no venereal disease, and always been perfectly healthy.

Previous History—Had been well up to two months ago, when he sought medical aid on account of "gastritis and diarrhœa." Has been *constipated* for the *past two years*. Before this regular. Constipation gradually grew worse, so that he had to take increasing doses of cathartics. He could and often did go for a week without having a movement of the bowels. When he did take medicine to open the bowels, he *did not have any pain at all. He has had no pain at any time in the abdomen* until the past two weeks, and this pain was around and above the umbilicus. During the past few months he noticed that when his stools were hard that the feces were pencil-shaped. There has been *no blood, pus* or *mucus*. Within the past four or six weeks he has had a *diarrhoea*. There was gas in the bowels and gastritis, as he called it, of his stomach. The man looked well and strong. Color good. Cheeks slightly sunken but not emaciated. Lips red, conjunctivæ normal.

Abdomen.

The first day of admission his abdomen was prominent in the epigastrium, with tympany, splashings, and gurgling on pressure. The abdomen below the umbilicus was not distended. There was no localized pain or tenderness at any point, but the muscles were in a state of irritation, so that it was impossible to make deep pressure at any point in the abdomen. Not that it hurt him, but that his muscles involuntarily contracted. There was no emaciation, although the man was thinner than usual he stated, no cachexia, no tumor. But on the history of digestive disturbances, increasing constipation, small stools, colics growing worse, the evidences that there was some form of intestinal obstruction were conclusive. The characteristic distention appeared after the second day, beginning low in the abdomen, filling up the left flank and gradually dilating the large intestine showing that the cause must be low down in the colon. In spite of of the absence of the specific cancerous symptoms nothing but an annular carcinoma would answer all the conditions so well. The diagnosis was then made of an annular carcinoma involving the lower end of the colon.

April 16th—The abdomen was opened up in the median line below the umbilicus. The intestines were only moderately distended. The growth was an annular carcinoma (adeno-carcinoma) deeply creasing the bowel, with no growth of tumor beyond the normal calibre of the intestine. The lymphatics were not involved. Excision of the mass was easy. There was, however, not enough of the rectum left to form an end-to-end anastomosis. The lower end was then ligated (Lilienthal's method) with catgut No. 3 chromic, and its end cauterized with carbolic acid, and allowed to retract into the bottom of the recto-vesical fossa. An inter-muscular incision was made opposite the anterior iliac spine and about one and one-half inches above Poupart's ligament. The proximal end of the sigmoid was fastened in this incision, and a large drainage tube fixed into the bowel by a purse-string suture to prevent soiling, which it actually did. Time of the operation, 50 minutes.

Everything went along all right with the patient until the 20th, when he rapidly developed general pulmonary edema, and died on the 21st. His abdominal condition was absolutely perfect.

The pathological report showed the tumor growth to be an adeno-carcinoma, involving all the coats of the intestine *except the serosa*.

SOME CASES OF URETHRAL CALCULI.*

JAMES R. HAYDEN, M.D.

My object in reporting the following cases of "urethral calculi" or concretions, is with the hope that they may shed some additional light on the etiology of these rather infrequent foreign bodies.

CASE 1—Thos. McB., 38. Admitted to Bellevue Hospital August 27, 1908, for painful and difficult urination.

Patient has never had urethritis. Eight months ago had a very severe attack of left renal colic, which has recurred at intervals. Two and a half months ago had last attack of colic, during which he felt something coming down from the left kidney to the bladder, and one week later and without pain he passed a small stone by the urethra; this was lost.

Examination—The urine is clear and contains flakes. No stricture detected. A bougie à boule touches a rough body in the bulbous portion of the canal, which can also be felt on palpation.

Treatment—External urethrotomy was performed in the usual manner and a 15 grain stone (see Plate I, Fig 1), removed from the bulb. The bladder was drained with a large soft rubber perineal tube for 24 hours, the patient making a prompt recovery.

This stone probably formed in the left kidney and on its outward course became engaged in the bulbous urethra where it remained until its removal.

An x-ray of the urinary tract was negative.

CASE 2—Thos. F., 45. Admitted to Bellevue Hospital December 14, 1908, for frequent, painful and difficult urination.

Patient had urethritis thirty years ago. Has had frequent attacks of complete urinary retention, relieved by catheter, and at present his stricture is being dilated with bougies. No history of renal colic.

Examination—The urine is very turbid from pus, and neutral in reaction. Four inches from the meatus is a stricture admitting a No. 24 F. endoscopic tube, projecting into which can be seen the end of a conical stone, which can be readily felt from without.

Treatment—External urethrotomy having been performed and the stricture cut, a 49 grain stone (see Fig. 2), was removed, and the bladder drained for 24 hours. Recovery prompt.

This stone probably formed behind the stricture, where it increased in size.

CASE 3—H. H., 45. Admitted to Bellevue Hospital December 11, 1908, for painful and difficult urination. No history of renal colic. Urethritis twenty-seven years ago, which patient says has never been cured. Eighteen, and again fifteen years ago internal and external urethrotomy were performed for the relief of strictures. Five years ago litholapaxy was performed *without an anaesthetic* and since that time patient has had painful, frequent and difficult urination, the stream stopping suddenly and temporarily at times.

Examination—The urine is cloudy and contains tissue elements. A No. 22 F. endoscope shows a stone in the bulbous portion of the canal, beyond which is a tight stricture.

Treatment—A stone weighing 26 grains (see Fig. 3), was removed through an external urethrotomy incision, the stricture cut and the bladder drained for 24 hours. Recovery satisfactory.

In this case a fragment of stone was left in the bladder after litholapaxy and passing into the urethra lodged behind the stricture.

CASE 4—Ed. O'C., 63. Admitted to Bellevue Hospital November 3, 1907, for very difficult and painful urination.

Patient has never had renal colic. Fifty years ago he had a very severe attack of urethritis, which lasted for two years. Eighteen years ago had acute retention of urine which was relieved by suprapubic aspiration. Two years ago began to have severe pain in the bladder, which was increased by motion, and at times has had complete stoppage of the stream.

Examination—The urine is very foul, alkaline and ammoniacal. Two inches from the meatus is a stricture, admitting a No. 14 F. bougie à boule, and a filiform stricture at the bulbomembranous junction, behind which the filiform grates upon a rough body, which can be palpated from the perineum.

* Reprinted from the American Journal of Urology, January, 1910.

Treatment—A stone weighing 11 grains (see Fig. 4), was removed through an external urethrotomy wound, the strictures cut, and the bladder drained for 48 hours. Recovery was uneventful.

In this instance the stone had its origin behind the stricture and remained there unnoticed until patient's admission to hospital.

Case 5—W. G. C., 63. Admitted to Bellevue Hospital December 30, 1904, for retention of urine.

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Patient gives no history of urethritis, or renal colic. Six weeks before admission patient began to have frequent, painful and difficult urination, and for the last three days all of the urine has been drawn by catheter.

Examination—The bladder is markedly distended (see Fig. 5). Temperature 101° F. Pulse and respiration normal. A bougie à boule touches a hard body just beyond the navicular fossa and on palpation four hard bodies could be felt in the pendulous urethra.

Treatment—The urethra was anæsthetized as completely as possible with 2 per cent. alpyin solution, and warm sterile oil injected, after which the four stones (see Fig. 6),

were removed by means of a urethral scoop and manipulations from without, the distal portion of the canal being compressed to prevent the calculi from slipping back. A full size catheter was then passed to the bladder from which was drawn 53 ounces of foul urine. The bladder was irrigated with boric acid solution, one pint of which was left in to prevent collapse of the distended and congested walls. All of the urine was drawn by catheter until the urethral abrasions healed, the patient taking plenty of bland water and urotropin and the canal being irrigated with mild astringent solutions. Recovery was uneventful.

In this case the origin of the calculi cannot be positively stated.

The x-ray was negative.

Case 6—A. V., 50. Admitted to Bellevue Hospital February 4, 1909, for retention of urine.

No history of urethritis. Has had several attacks of renal colic during the last two years. Twenty-four hours before admission patient had a very severe attack of left renal colic, which was followed by agonizing pain in the perineum and very difficult urination which resulted in complete retention a few hours before his admission.

Examination—The bladder is moderately distended. A 25 F. sound detects a rough body in the prostatic urethra, where it was too firmly held to be pushed back into the bladder.

Treatment—Through an external urethrotomy incision two stones weighing 17 grains (see Fig. 7), were removed from the prostatic urethra with great difficulty, as they were firmly grasped by the walls of the canal. The bladder was drained in the usual manner. Recovery was prompt and satisfactory. X-ray plates were negative.

This stone was undoubtedly renal in origin, and grasped by the prostatic musculature during the patient's efforts to void his urine.

Urethral forceps were not employed in any of the above cases, as in my experience calculi and rough foreign bodies extracted from the deeper portions of the urethra in this manner are liable to lacerate the urethral walls to a considerable degree, whereas a simple external urethrotomy incision allows inspection of the foreign body, plenty of room for its delivery, and being longitudinal, heals promptly without stricture formation, provided the wound is dressed daily by the surgeon himself, and the urine rendered sweet and copious by plenty of water and urotropin.

If the calculus is situated in the *pendulous* urethra, it can then be removed with forceps or scoop, aided by manipulations from without, or if the concretion is small, the forceps can be worked through an endoscopic tube, the operative field being brilliantly illuminated.

The conclusions to be drawn from the above cited cases are:

First, the importance of freeing the bladder of all fragments of stone after cutting or crushing operations, to prove which a cystoscopic examination should be made after litholapaxy, and every portion of the bladder mucous membrane examined with the bare finger after cystotomy.

Second, always examine the canal for concretions behind strictures, but especially in old and tight ones, and those complicated by fistulous tracts.

Third, during and after an attack of renal colic all of the urine should be saved and examined for sand or concretions, and if neither are found, the urinary organs should be subjected to the "x-ray" or instrumental examination.

Fourth, litholapaxy, especially for large stones, can be performed in a more thorough manner when the patient has general anæsthesia, and the surgeon does not hurry to spare his patient the pain of a proper post-operative examination.

THE PERSISTENCE OF THE GONOCOCCUS IN THE PROSTATE.*

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The persistence of gonococcus infection is a subject which touches some of the most important problems with which we have to deal in our daily practice. While much study has been devoted to this theme, there are even now, thirty years after

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Neisser's discovery of the gonococcus, many phases of the subject that are still imperfectly developed.

The general proposition that the prostate is frequently the seat of a persistent gonococcus infection will doubtless be agreed to by all urologists. When we come to inquire, however, how frequently is the prostate thus invaded; how often and how long does the invasion persist; how is its persistence diagnosticated, and to what extent and by what means is it curable, we at once meet with a variety of views.

It is with the purpose of placing before you the results of a careful study of 180 cases of gonorrhœa with reference to the presence and persistence of gonococcus infection in the prostate, that I present this paper for your consideration. The material was taken from my private practice, and includes twelve cases referred to me by other physicians.* I found it impossible to watch hospital or dispensary patients closely enough to draw conclusions.

1. Method of Examination.

(*a*) *Obtaining the Prostatic Secretion*—The patient was asked to report with a full bladder, and the Kollmann "five glass test" was applied. Special attention was paid to the third glass (shreds, etc., from the posterior urethra), and to the fifth glass (plugs from the prostate, squeezed out at the last stage of urination). The genitals were thoroughly scrubbed with green soap and water. The anterior and the posterior urethra as well as the bladder were then thoroughly and repeatedly washed with sterile water, about 100 c.c. of the last wash water being left in the bladder. The prostate was massaged, care being taken to press on the perinæum with the knuckles, and any secretion appearing at the meatus was caught on a slide. Usually there was enough secretion obtained thus for microscopical examination. If nothing flowed from the meatus, the patient was asked to walk around the room once or twice. The urethra was at no time "milked," as this might bring down some hidden germs from its glands.

There is no doubt that the secretion sometimes flows back into the bladder during the massage, or that it may be scanty and remain in the posterior urethra. In such cases no fluid comes from the meatus, and there is nothing to do but to allow the patient to void the rest of his wash water, which had been left in the bladder to provide for this contingency. The sediment in the wash water may then be centrifuged and examined. I realize that there are loopholes for errors in this technique—principally because it is practically impossible to wash out the urethra so thoroughly that it will be entirely free from germs.

For the practical purpose of an examination intended solely as a clinical index to diagnosis, prognosis, and treatment, the method outlined, in my humble opinion, is entirely sufficient. Admittedly, it will not stand the scrutiny of exact bacteriology, yet it was justified because I sought only working data, not absolute bacteriological perfection.

When cultures are made, on the other hand, the technique of pure bacteriology must be used. There is then no excuse for clinical makeshifts. For this reason in all cases in which I made cultures, I followed scrupulously the technique of Young, Geraghty, and Stevens (1)—the most perfect hitherto described, though still imperfect as their own results show:—After thoroughly washing the anterior urethra as above described, a sterile urethroscope was introduced, its tube was thoroughly flushed with sterile water, and the prostate massaged. A sterile platinum loop was used for obtaining the prostatic fluid at the bottom of the tube, and for inoculating the culture media.

(*b*) *"Provocation" or Bacteriotaxis*—The use of irritant solutions as a "provocative measure" to bring out latent gonococci is an old and tried method. Neisser (2) in 1883 recommended irrigation of the urethra with a 1 in 20,000 mercuric chloride solution to act as an irritant that might bring out hidden gonococci, along with a reactive discharge. Janet (3) in 1892 advised the use of a one per cent. solution of silver nitrate for the same purpose, while Hogge (4) went so far as to declare that other diplococci were killed with either of these solutions, and that the "provocative test" was a sure way of determining whether gonococci were hidden anywhere along the canal. Finger (5) speaks of "provocation" with from one-half to one per cent. solution of silver nitrate applied with an Ultzmann syringe, and emphasizes the need of repeatedly using this test, and also of examining the prostatic secretion after its use.

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* In addition to this clinical material, I have records of examinations of prostatic secretion in 140 cases in which specimens were submitted to me by other physicians. As I have no clinical data on these cases, I did not include them in the present study. I take opportunity to acknowledge my indebtedness to Dr. A. L. Wolbarst, of this city, who sent me the largest number of these slides in the course of a year, and who will present a paper dealing with his own cases at this meeting.

The "provocative" method has remained in use in spite of numerous criticisms as to its trustworthiness. Orlowski (6), in speaking of Alexander's (7) modification of this method (the use of hydrogen peroxide instead of silver nitrate) in particular, and of the irritative reaction in general says that "provocation does not provoke"; that it is harmful, produces postgonorrhœal catarrh, and is untrustworthy. There is some justice in his criticism, and the use of "provocative injections" as a routine measure must be frowned upon. When properly used, with due care, they are of considerable service, and have never done any harm in my hands. The reagent used was a one per cent. solution of silver nitrate, of which fifteen drops were injected into the posterior urethra with the aid of an Ultzmann syringe. If a morning drop showed the next day, it was examined. In any case the prostate was massaged within twenty-four or thirty-six hours after the injection and the secretion examined.

The value of the method is especially evident in cases of prostatitis of long standing in which, if any gonococci exist, they fail persistently to appear in the massaged secretion. I shall speak a little further on of my results with this method.

(*c*) *Technique of Staining**—The smears were spread as thinly as possible, sometimes adding a little water before the material had time to dry. The dry smears were fixed with alcohol and ether (equal parts poured on the slide and allowed to evaporate for fifteen to thirty minutes) and stained with aqueous eosin and methylene blue, as described in my previous paper, dealing with vesicular material in massage urine (9).

In preference to this method, I have used during the past year, a double stain consisting of eosin and of methylene blue in absolute methyl alcohol. The principle of this method is that of the well known Romanowsky-Nocht (11 and 12) stain, with the difference that the stain is mixed freshly when needed. The method is identical with that used by Tiedemann (14) for blood, recently recommended by Cook (15), and is similar to the blood staining method used by Harlow (16), Peebles (17), and Hayhurst (18).

No previous fixation is required. The *thinly spread* smear is dried, and equal parts of the following solutions are mixed in a test tube, which must be *chemically clean*, i. e., free from traces of acids, alkalis, or organic matter. The slightest contamination causes a precipitate and destroys the stain:

I. Aqueous Eosin (Grueb'er, "W. G.") 1.0;
Methyl alcohol, c. p. "Reagent," (Merck's) .....100.0.
II. Methylene blue, pure, medicinal (Gruebler) 1.0;
Methyl alcohol, c. p. "Reagent" (Merck's) .....100.0.

Note—Keep in separate well stoppered bottles, away from acid fumes, etc.

A few drops of the mixed solutions are poured upon the smear and allowed to remain for one minute. Then about four times the volume of distilled water is added, and the slide is allowed to remain thus covered for five minutes. The smear is then drained, washed in distilled water, dried, and examined.

The result is a brilliant contrast stain, showing blue nuclear material and bacteria against a pink background of matrix and cell bodies. The eosinophile cells show distinctly. The gonococci are stained deep bluish black. The morphology of both cells and bacteria shows very sharply, and the degenerated epithelia and broken down pus cells met with in chronic prostatitis can be readily recognized.

Gram's Stain—While the stain described is excellent for the morphological study of prostatic secretion, Gram's stain is indispensable for the differentiation of gonococci. *Gram's stain is worthless unless properly applied,* and unfortunately its proper technique is not taught in any of the textbooks which I consulted. For this reason I may be permitted to call attention to some points of importance in the use of Gram's stain.

From personal experience, I have come to reject practically all modifications of the original Gram's method as untrustworthy. I would especially warn against the use of acetone alcohol (Nicolle's method) for decolorizing, as this reagent may also decolorize Gram positive cocci. The best decolorizing agent is absolute alcohol (20, 21, 22), because it has an unvarying strength (if properly kept, with anhydrous copper sulphate in the bottle, to absorb water). The directions usually given: "Decolorize until no more violet color comes off" are wrong. The absolute alcohol should be used only for thirty seconds. If used longer, it begins to decolorize the Gram positives.

Furthermore, one must remember to avoid *understaining* with aniline (or carbol) gentian violet, and to avoid *overstaining* with the contrast color. The contrast stain

* This is a brief summary of this subject. The full account of the technique of staining and of preparing cultures will appear in the *Transactions of the American Urological Association,* 1909.

best suited for routine work is dilute Bismarck brown. Fuchsin is confusing if there has been any overstaining with it, as the very deep red cocci cannot be readily distinguished from the purple germs.

The most satisfactory results are obtained as follows (thin smears are a *sine qua non*): 1. Stain with strong carbol gentian violet for one and a half minutes. 2. Drain, and at once apply Gram's iodine solution; drain, and reapply the same repeatedly for a minute and a half. 3. Drain, and decolorize for thirty seconds in absolute alcohol. 4. Counterstain with dilute Bismarck brown. 5. Wash in water, dry, mount.

(*d*) *Cultures*—The criticism will be made that the appearance of a typical Gram negative diplococcus does not necessarily mean that we are dealing with the gonococcus of Neisser (25). That a cultural proof is desirable I readily admit; that it is necessary ordinarily for clinical purposes, I doubt strongly. The fact that Finger, Steinschneider, and Galewski (26) found a Gram negative diplococcus which was not a gonococcus only in 4.6 per cent.—4.8 per cent. of a large series of cases, shows that in 93.2 per cent. of cases we are right in saying that we deal with the gonococcus, after the examination of a Gram stained smear. In women the pseudogonococcus has been found more frequently, but in men a Gram negative diplococcus of typical appearance must be considered guilty of being a gonococcus until proved innocent, with the chances of about 95 out of 100 that the prisoner is guilty.

Cultures were taken in thirty-eight of the total number of my series of cases. Of these nine gave positive, the rest negative results. Of the positive cases, six were between eighteen and twenty-four months' duration, the rest were of more than two years' duration.

It is very easy strenuously to insist on cultures, but it is very difficult, even for the most experienced bacteriologists, to cultivate the gonococcus in a case of chronic prostatitis. This difficulty increases when the material used contains comparatively few of the germs (as is the case in all chronic types of gonorrhœal infection), and when the germ is in the state known as "degeneration form."

Cultures, moreover, sometimes give negative results when the gonococcus is found morphologically. The idea that there was something specific in "the culture test," i. e., that if one made a culture on a special medium good for gonococci and if a growth occurred on this medium that looked like the gonococcus, one had a true blue Neisserian coccus, and that if nothing grew, no gonococci were present—this idea, I say, has been exploded long since. Cultures of gonococcus are only valuable *when successful*, for the purpose of isolating and identifying the germ. When negative they mean absolutely nothing, as the gonococcus is so capricious that it often will not grow even upon media specially suited to its growth. (Wertheim, 27, Schanz, 28).

On the other hand, even when apparently positive, cultures must be very carefully studied and the results checked by a competent bacteriologist. We need only cite the fact that staphylococci when grown upon media specially suitable for gonococci have a tendency to assume the diplococcus type and to look like coffee beans (Paltrock, 22). Van Calcar and Gotte (29) found recently that they could cultivate staphylococci in a form resembling gonococci and that after a few generations they no longer grew upon ordinary media, but only upon blood agar or ascitic agar, like gonococci. By inoculating cultures of these atypical staphylococci into dogs, these authors produced a urethritis with a purulent discharge containing intracellular diplococci looking exactly like gonococci.

Ascitic agar (plate method, with three streaks) has given me the best results. There are cases, undoubtedly, in which cultures show the presence of gonococci, when smears fail to do so, but to make up for these cases, there are some in which the culture fails and the smear is successful when the examinations are numerous enough. With the most careful technique, and with the most expert advice at my command, this has been my experience.

II. Frequency of Prostatitis as a Complication of Gonorrhœa.

While H. von Zeissl (30), as early as 1879 declared that "no gonorrhœa could exist for any length of time without involving the prostate," the tendency of most writers in the eighties was to consider gonorrhœal prostatitis as one of the rarer complications of urethritis. Within the past fifteen years, the frenquency of prostatic involvement has come to be regarded as very great, and some authors go so far as to say that "prostatic infection is practically synonymous with chronic gonorrhœa."

The table herewith presented (Table I) shows at a glance the marked variations in the estimates of different authorities as to the frequency of gonorrhœal infection of the prostate.

TABLE I.

Frequency of Gonorrhoeal Prostatitis.

Year	Author	Frequency Among Gonorrhœas.
1903	Guyon (31)	Rare.
1890	Fürbringer (32)	Rare.
1891	Ballou (33)	3 per cent.
1894	Peterson (34)	16 per cent. to 20 per cent.
1895	Colombini (35)	36 per cent. in acute; 28 per cent. in subacute; 40 per cent. in chronic.
1899	Goldberg (36)	33 1-3 per cent. to 50 per cent.
1903	Wossidlo (37)	ditto.
1905	Bierhoff (38)	49.5 per cent. (100 per cent. in posterior urethritis).
1904	Notthaft (39)	58 per cent.
1903	Bonn (40)	68 per cent.
1885	Montagnon (41)	70 per cent.
1896	Eraud (42)	70 per cent.
1896	Pezzoli (43)	80 per cent.
1903	Waelsch (44)	81 per cent. (94 per cent. in posterior urethritis).
1903	Casper (45)	85 per cent.
1879	Von Zeissl (46)	Very frequent.
1884	Neumann (47)	
1889	Posner (48)	
1893	Bransford Lewis (49)	
1896	Rosenberg (50)	
1900	Chetwood (51)	
1900	Valentine (52)	
1900	Porosz (53)	
1905	Finger (54)	
1905	Frank (55)	
1906	Von Frisch (56)	
1906	Young (57)	

This apparent conflict of opinions, upon analysis, may be accounted for by several factors:

1. Most of the authors quoted who found prostatitis *rare* depended entirely upon palpation for their diagnosis.

2. Some of them found low percentages because they erroneously regarded prostatorrhœa as an essential symptom of prostatitis.

3. The most important factor in the variability of the figures is the *duration* of the gonorrhœal infection; for, as will be shown later, prostatitis is most frequent in the very chronic cases.

4. Authors do not always state how many cases of posterior urethritis there were among their cases.

In my own material, which comprised 180 cases of chronic gonorrhœa carefully watched in private patients, I found 108 cases of prostatitis, i. e., sixty per cent. The chief criterion for diagnosis was the examination of prostatic secretion, but thorough palpation was never neglected. No case was diagnosticated as prostatitis in which there were not at least a fair number of pus cells in the prostatic juice, or else sufficiently marked palpatory signs. My figures, therefore, agree approximately with those of Notthaft (39) and are somewhat higher than those of Bierhoff (38), Goldberg (36), and Wossidlo (37).

The frequency of prostatitis in my series varied with the chronicity of the infection, as the following table shows:

TABLE II.

Frequency of Prostatitis in Relation to the Chronicity of the Infection.

Duration since last infection.	Gonorrhœa: Cases.	Prostatitis: Cases.	Per cent.
6 to 12 months	73	39	53
12 to 18 months	54	31	58
18 to 24 months	27	18	64
2 years and over	26	20	77
Total	180	108	60

It will be seen, therefore, that the percentage of prostatic infections increases with the chronicity of the case. The high percentage found in cases of over two years' duration (seventy-seven per cent.) was perhaps partly due, however, to the special attention and care bestowed upon these cases in examining the prostatic secretion many times, although this percentage is but slightly higher than that found by other authors, e. g., Notthaft (39), who found prostatitis in seventy-two per cent. of his advanced cases of gonorrhœa.

III. Relation of Prostatitis to Posterior Urethritis.

It may seem plausible to assume that in every case of prostatitis there must also be a posterior urethrititis. This, however, does not seem to be necessarily the case. Notthaft (39) found the prostatic urethra free from lesions in 52 per cent. of his cases of gonorrhœal prostatitis (the five glass test being used). In my own series, the five glass test showed a clear posterior urethra in only 15 per cent. of cases, while in the remaining 85 per cent. there was posterior urethritis.

While posterior urethritis, therefore, is probably found with prostatitis in the great majority of cases, the two conditions do not necessarily occur together. It must be noted, however, that some authors (Finger (5), Frank (55), Bierhoff (38), and Waelsch (44) found prostatitis in practically every case of posterior urethritis, so that if the cases of posterior urethritis, as such, be picked out, we are almost certain to find prostatitis, while the converse need not necessarily be true.

There is some authority, perhaps, for the supposition that a primary infection of the prostate may take place, the gonococci passing directly into the prostatic ducts during coitus (Neisser (25), Putzler (58), Pezoli (43), and others). Still other authorities suggest the possible skipping of the posterior urethra (Goldberg (36), Notthaft (39), etc.) by the infection, which jumps from the anterior urethra directly into the prostate. While there may be some facts in support of this theory, it seems to be somewhat less plausible than the simple explanation which satisfies the conditions met with; namely, that the posterior urethritis has healed, while the prostatitis persists in those cases in which the latter alone is found.

IV. Occurrence of the Gonococcus in the Prostatic Secretion.

The great differences in the findings of various authors in their cases of gonorrhœal prostatitis appear in the following table:

Table III.

Occurrence of Gonococcus in Prostatic Secretion.

Author.	Cases of gonorrhœal prostatitis.	Gonococci found in	Per cent.
Frank (41)	210	179	85.5
Bierhoff (38)	151	127	84
Notthaft (39)	120	47	39.2
Le Fur (59)	38	4	10.5
Bonn (40)	50	3	6
Hinrichsen (60)	35	0	0
Young (1)	17	0	0
Cohn (61)	12	0	0

Upon analysis, I found that these differences in the results obtained by such trustworthy authors were due principally to the various proportions of early and very chronic cases included in each series. Thus, in Frank's series, there were ninety-six cases (out of 210) in which the duration since the onset of gonorrhœa was less than eight days. Bierhoff in his excellent paper does not state the number of cases in his series which had lasted less than six months since the infection, but as his cases range up to thirty years' duration, his series must have included all stages. Notthaft's series included only cases of over six months' duration, and shows a materially smaller percentage with gonococci. The other authors mentioned reported chiefly cases of the more chronic type.

In my series of 108 cases, all of which were considered only after at least six months had elapsed since the last infection, there were gonococci in thirty-one cases, i. e., in 28.7, a percentage lower than that of Notthaft (39 per cent.).

That the frequency with which gonococci are encountered in the prostatic secretion diminishes markedly with the chronicity of the infection (taking always the last

attack of gonorrhœa as the supposed starting point) is shown strikingly in my series of cases:

TABLE IV.

Occurrence of Gonococci in Relation to Chronicity of Infection.

	Duration since last infection	Cases.		Gonococci found in		Per cent.
I.	6 to 12 month	39		18		46
II.	12 to 18 months	31		9		29.0
III.	18 months to 2 years	18		2		11.2
IV.	2 to 3 years	7	20	0		
V.	3 to 18 years	13		2		
		108		31		28.7

The two cases in which gonococci were found in the last two groups were in patients in whom repeated examinations were made before the positive result was obtained. Most of the authors dealing with this question failed to state the number of examinations made. The gonococcus, however, is rarely found at the first examination of prostatic secretion in any case, especially in a case of over six months' duration. In my series of 108 cases, there were a total of 514 examinations made, i. e., an average of about five per case. Gonococci, or even pus cells, were often missing till the fourth or fifth examination. With the chronicity of the infection there is an increasing difficulty in finding the gonococcus, and in some cases as many as twelve or even eighteen examinations were made before a positive result was obtained.

V. VALUE OF BACTERIOTAXIS BY MEANS OF PROVOCATIVE INJECTIONS.

Provocative injections (see above) were given in my cases only after at least three negative examinations. In all, eighteen cases received provocative injections, and of these only six showed the presence of gonococci after the injections. In four of these cases, the gonococci disappeared within a week and reappeared upon the second provocative injection, while in the remaining two cases gonococci could not be brought out by a second provocative injection given about two weeks after the first.

Of the eighteen cases in which provocative injections were used, four were examined between three and eighteen years after the last gonorrhœal infection, six between two and three years, four between eighteen and twenty-four months, and four between twelve and eighteen months after infection. Provocative injections were not given in any case of less than a year's duration.

While these injections did not seem in any case to produce any harmful effects, due caution was used in applying them. The cases selected for this purpose were always those in which there was some particular reason for making sure that no gonococci were present, for instance, impending marriage, etc.

As will be seen from the figures given, these injections did not always produce the desired effect so far as the bringing out of the gonococci was concerned, but even in the limited number of cases in which they assisted in the examination, they were of considerable value. In no case were gonococci found after the injections were discontinued, when the massaged secretion after injection had given a negative result. This, however, does not prove that the injections are by any means infallible, as the number of cases in which these reactive tests were used was intentionally small.

VI. PERSISTENCE OF THE GONOCOCCUS IN THE PROSTATE.

Here again, the statements of those who have studied this question during the past ten or fifteen years vary markedly. Some of the earlier authors, particularly Finger (5), Neisser (25), Putzler (58), emphasize the length of time during which the gonococcus may be found persistently in the prostate. On the other hand, the tendency of the later writers is to regard the presence of the gonococcus as rare after one or two years. Cohn (61), Wossidlo (37), Goldberg (38), and Notthaft (39) may be mentioned among this latter group. Goldberg regards the gonococcus as very rare after the first year, Notthaft found it rarely after two years and never after three years. A number of cases, however, have been reported in which the gonococcus has been found five years or longer after the last gonorrhœa. In my series, there were two cases that came under this heading.

In one of these cases the gonococcus was found fourteen years after infection, in the other five years after infection. In both instances, provocative injections of silver nitrate (15 drops of a one per cent. solution) were required to bring out the germs.

In the first of these cases, the patient was a sexual neurasthenic with "gonorrhœophobia," who had practiced *coitus condomatus* ever since the apparent cure of his infection fourteen years previously, so presumably there had been no symptomless reinfection of the prostate. In spite of repeated efforts, cultures were unsuccessful, but morphologically the germ was typical and it was decolorized with Gram's stain.

The second patient was a man about town who had been frequently exposed to reinfection but who had never had a discharge since his first and only attack, five years previously. This case is not so valuable as evidence of the persistence of gonococcus, because the possibility of a symptomless reinfection cannot be excluded. In this case cultures were made on ascitic agar, proving the diplococcus to be positively the gonococcus.

VII. Mixed Infection in Gonorrhoeal Prostatitis.

A great deal of work has been done during the past decade with a view of determining the identity of the germs other than the gonococcus, which are concerned in the infection of the prostate. It would lead me too far to review the extensive literature of the subject. In spite of the amount of work which has been done, there does not seem to be very much definite knowledge available as to the pathogenic rôle of the numerous bacterial species found in the causation of prostatitis. We are concerned here with mixed infection solely as pertaining to prostatitis of gonorrhœal origin. In my work, no attempt has been made to cultivate and isolate the various germs found in the prostatic secretion, but a careful search was made in all the smears for any bacteria that might be present in each case. From a study of my cases of prostatitis of gonorrhœal origin, I have been impressed with the great frequency of mixed infection, particularly in cases in which the gonococcus could not be found.

The relation between mixed infection and the chronicity of the gonorrhœal infection, or with the lapse of time since the last infection, is shown in the following table:

Table V.

Mixed Infection in Prostatitis of Gonorrhoeal Origin.

	Duration since last infection.	Number of cases examined.	Gonococci alone.	Gonococci and other germs.	Other germs alone.	Germs absent.	Total mixed infection. Cases.	Per cent.
I.	6 to 12 months.....	39	5	13	19	2	32	82
II.	12 to 18 months.....	31	0	9	18	4	27	87
III.	18 to 24 months.....	18	0	2	16	0	18	100
IV.	2 to 3 years.....	7	0	0	7	0	7	100
V.	3 to 18 years.....	13	0	2	6	5	8	61.5
	Totals	108	5	26	66	11	92	85

It will be seen that gonococci were present *alone* only in the earlier types of cases up to one year. Mixed infection (85 per cent. of cases) is a prominent factor from the first, and is present in a large percentage of cases in all stages of chronicity. How much of this mixed infection is secondary to instrumentation, I am unable to say, but I found, like Notthaft (39), Goldberg (36), and others that the gonococcus seems to disappear after a few years and is replaced by a number of other germs. In the very chronic cases, it is very much more common, therefore, to find these associated germs than to find the gonococcus.

The subjoined table shows the individual types of germs found in my cases, and the frequency with which each morphological type occurred. No attempt was made at accurate bacteriological definition.

Table VI.

Types of Bacteria Found in 108 *Cases of Gonorrhoeal Prostatitis.*

A. *Gonococci*—31 cases.

I. Gonococci alone. 5 cases.
Gonococci plus other germs, 26 cases.

B. *Other Germs*—92 cases.

II. Staphylococci .....67 cases, 74 per cent.
Often in very small groups.
Rarely abundant.
Sometimes as isolated cocci.

III. Bacilli .....25 cases, 28 per cent.
Various types and sizes, often short, with rounded ends (colon bacillus?); Gram negative. Sometimes thinner, longer bacilli in large numbers, resembling pseudodiphtheria bacillus.

IV. Gram positive diplococci.....9 cases, 10 per cent.
Rarely of same size as gonococci.
Never intracellular.

V. Streptococci .....7 cases, 7.6 per cent.
Rarely numerous, in short chains of fairly large cocci.
Sometimes in longer chains, smaller cocci.

VI. Other, unclassified germs.....6 cases, 6.5 per cent.

C. *No germs found.* 11 cases (12 per cent.).

The total number of findings of mixed infection was 118, among ninety-two cases, i. e., there were twenty-six cases with more than one germ present. The staphylococcus in some form was by far the most frequent germ, an interesting fact, particularly because it is apt to be mistaken for the gonococcus when it assumes the diplococcus (coffee bean) type already mentioned in speaking of cultures.

VIII. Relation of Clinical Data and Microscopical Appearances.

The absolute need of microscopical examination of the prostatic secretion in the diagnosis of gonorrhœal prostatitis was strikingly shown in my series of cases. While there were microscopical findings justifying the diagnosis of prostatitis in 108 cases (germs and pus, ninety-seven cases; pus alone, eleven cases), there were thirty-eight cases (about thirty-five per cent.) in which palpation showed absolutely no changes in the prostate. Furthermore, subjective symptoms, including neurasthenia, various pains, frequent desire to urinate, etc., were present in seventy-nine and absent in twenty-nine cases (twenty-seven per cent.). The urine was perfectly clear in thirteen cases (twelve per cent.) in which the prostate was found the seat of inflammation, and in five of these there were gonococci and other germs found. The occurrence of prostatitis with perfectly clear urine is by no means a new fact. It is, therefore, impossible to exclude prostatitis by clinical examination alone.

IX. Treatment.

Although I do not here intend to go into details of treatment, the following summary may not be amiss. Massage of the prostate is by far the most useful measure in chronic cases. The use of heat in the rectum is of value and may be applied with the aid of a double current rectal tube, carrying a stream of hot saline solution. Prolonged irrigations of the prostatic urethra by means of weak silver nitrate solution (1 in 16,000 to 1 in 5,000), applied with the prostatic douche tube may alternate with the massage, and are especially useful in combating the subjective symptoms (pain, urinary disturbances, sexual neurasthenia, etc.). After each massage an irrigation with weak silver nitrate solution in the cases with gonococci, or with some other solution, e. g., mercuric oxycyanide, in cases with mixed infection is to be given as a routine measure. Suppositories have never given me any appreciable results in chronic prostatitis, and probably do not reach the prostate at all. The treatment should not be interrupted suddenly, but should be gradually discontinued. General tonics, an ample diet, and general hygienic measures should not be neglected.

X. Curability of Gonorrhœal Prostatitis.

Upon this point there are just as many varying opinions as upon some of the points previously discussed. We find, for example, that some authors assert to have cured all their cases of gonorrhœal or postgonorrhœal prostatitis, while others pessimistically declare this condition to be practically incurable (Neisser, 25, Goldberg, 36).

The question is, what constitutes a cure? Some say, "when no more gonococci can be found in the prostate"; others declare that so long as any pus cells are present in the secretion, there is no real cure. The former have larger percentages of cures, the latter very small percentages. To remove every pus cell from the prostate secre-

tion, it will be admitted, may take months and years of persistent treatment. To my mind, this would be carrying things to extremes, and I personally am satisfied when all germs have vanished, when the number of pus cells has been reduced to a very small one, when the patient has no symptoms, and when his urine is clear. Repeated and careful examinations by a competent man are needed to exclude gonococci, and provocative injections may be used as a last resort. If all these points are satisfactorily settled, there is no use of keeping up treatment, even if the patient has occasional pus cells in the prostatic secretion. Judged by this standard, cases of gonorrhœal prostatitis are curable in the very great majority of instances in a reasonable time.

XI. Consent to Marriage.

From the data presented, it appears clearly that the gonococcus can persist for a long time in the prostate, although it is exceptional to find it lurking in that stronghold longer than two years after infection. We should be as cautious as ever in giving our consent to a man's marriage whenever a history of gonorrhœa is given. Even when the physician has done the best he could to exclude the presence of gonococci, postmarital infection with its tragic consequences at times occurs. Repeated examinations, accurate technique, patience, and perseverance should be our watchwords in passing upon a man's fitness to marry, and we should only give our consent when, in conscience, we can say that the chances of a persistent gonococcus infection in the prostate—for this is usually the final refuge of the gonorrhœal germ—are *nil* so far as human skill and human mind can tell.

Summary and Conclusions.

1. Thorough irrigation of the urethra before massaging the prostate is essential in order to exclude contamination of the prostatic secretion by pus and bacteria from the urethra.

2. Injections of fifteen drops of a one per cent. solution of silver nitrate into the urethra twenty-four to forty-eight hours before prostatic massage sometimes reveal gonococci, when other means have failed.

3. A double stain of eosin and methylene blue in pure methyl alcohol, after the manner of the well known blood stains, is excellent in the morphological study of prostatic smears. Gram's stain is essential, but is misleading, unless properly applied.

4. Cultures, while desirable, are often unsuccessful, owing to the capricious character of the gonococcus. Negative cultures are not conclusive.

5. Of 150 cases of chronic gonorrhœal infection, from six months to eighteen years' duration, sixty per cent. showed prostatitis. The older the infection, the more frequent was the prostatitis.

6. Of the 108 cases of prostatitis, thirty-one, or 28.7 per cent., showed gonococci in the prostatic secretion. The older the infection the less probable was the finding of gonococci in the prostate. After three years, gonococci were found rarely, even after most persistent efforts. Many and thorough examinations are needed before we can be at all certain that the gonococcus is absent from the prostate.

7. Mixed infection occurred in eighty-six per cent. of the cases studied. The gonococcus alone occurred in only five cases of 108, and all five were cases of less than one year's duration. The older the case the more prevalent was the mixed infection. Staphylococci occurred in seventy-four per cent., bacilli in twenty-eight per cent., Gram positive diplococci in ten per cent., and streptococci in 7.6 per cent. of cases with mixed infection.

9. The absolute need of microscopical examinations of prostatic secretion was shown by the fact that palpatory signs were absent in thirty-eight cases (thirty-five per cent.), while thirteen cases (twelve per cent.) showed absolutely clear urine, although the smears showed prostatic infection.

10. Gonorrhœal prostatitis is curable by proper treatment in the great majority of cases.

11. Consent to marriage should not be given until all methods of examination have been exhausted, and until the possibility of a postmarital infection is practically excluded, in the present state of our knowledge.

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TUMORS OF THE BLADDER.*

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As a preliminary procedure in determining the nature of the surgical intervention to be followed in the above condition one should, by means of cystoscopic examination,

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ascertain the exact location, whether the cause for removal be single or multiple, pedunculated or sessile, villous or cauliflower, in appearance. The occasion for such examination in the vast majority of cases will prove to be an intermittent spontaneous hematuria; rarely, when the growth is located in the region of the vesical neck, the blood will be more marked at the end of urination. This hematuria is capricious, entirely independent of external causes, such as obtains in the case of vesical calculus; in fact, it frequently is more marked when the patient is resting in bed, disappearing and reappearing without discernible cause. There may be intermittent obstruction to the outflow by either the mass or fragments plugging the internal orifice, as observed in one case of papilloma. Occasionally, however, there may be a rebellious cystitis requiring cystoscopic examination which first reveals the presence of a vesical growth. Thompson has called attention to dysuria as an indication of malignancy; it would appear, however, to be more of a determining factor in cystitis than in the former.

For the cystoscopic examination it is best to employ an instrument carrying a direct and an indirect telescopic tube, thus giving a vertical as well as a horizontal picture. In this way one obtains a better idea as to the extent of the pedicle, a most important item in determining the mode of approach. Careful but thorough irrigation is a very important requisite in the conduct of this procedure, as, while it is proper when possible to undertake the examination in the interval of bleeding, nevertheless cases present themselves for diagnosis in which the hematuria is either so abundant as to require immediate intervention, or, as in a recent case under the observation of the junior contributor to this paper, of a gland-cell carcinoma with pedunculated outgrowths situated about the left ureteral orifice, and in which the hematuria was constant for forty days; while during nine months prior to this there had been complete absence of blood. This period followed three months of constant hemorrhage.

The irrigation is best conducted from a reservoir through a double-current tube, having a small inflow and a large outflow. By means of this appliance too sudden distention of the bladder is avoided, while the large outflow affords ready evacuation of the clot; and the addition of an adjustable diaphragm attachment permits of the leisurely interchange of the various telescopic tubes without the customary jarring, with its attendant traumatism.

Beyond ascertaining the exact situation, the extent of pedicle, and the size and general physical characteristics of the growth one should not go. Least of all should one attempt anything more than a tentative diagnosis, inasmuch as pedunculation is by no means a definite indication of benignancy (Albarran reports twenty-eight pedunculated growths, thirteen being benign and fifteen malignant); and not infrequently do pedunculated growths present themselves as outriders from a malignant base. Nor should much dependence be placed on the microscopic examination of particles spontaneously expelled, while frozen sections at the time of operation may be misleading; and the fact that an induration of the pedicle at its site of implantation may be the result of a hypertrophy of the connective-tissue element of a benign growth, rather than an indication of malignancy, serves to accentuate an already complex situation.

It is well to reinforce our cystoscopic examination with a stone-searcher exploration, as by means of this examination one may determine fairly accurately the degree of infiltration presenting in the growth. In three cases of vesical carcinoma coming under the observation of Dr. McCarthy, a correct diagnosis was arrived at in this manner. Rectal palpation should always constitute a step in the examination. It may be advisable to catheterize the ureters before operation. Inasmuch, however, as the growth in the majority of cases is situated near one or the other orifice this procedure is not infrequently found impossible, as there may be complete obstruction of the orifice by the neoplasm. In such event one should catheterize the ureter on the healthy side, to serve as a guide in locating the other. This should be attempted first with the indirect prismatic cystoscope. Failing in this the Buerger cystourethroscope, or the aspirating cystoscope of Luys may be employed. Should this prove unsuccessful the catherization may be conducted through the open bladder by means of the last-mentioned instrument. This operation should, however, be necessary only in the event of obstruction of the ureteral mouth by the growth, as with the present armamentarium one should hardly fail otherwise.

The operative procedure will depend upon the pathologic appearance, the location of the tumor, the type of attachment; and finally as to the number—whether one has a single growth or multiple ones to contend with. Those tumors or growths which to the examining eye present an appearance of infiltration about the pedicle, or about the margins in a sessile growth, should be as fully removed as those pronounced malignant; while in the soft pedunculated and sessile type excision through the mucosa is all that is necessary.

In regard to position, one cannot attack a growth in the immediate vicinity of the ureteral orifices without being prepared to do a new implantation. When multiple growths are present either a wide removal of the surrounding mucosa or a partial resection of the bladder may be found necessary. Pedunculated growths of an apparently benign character situated in the immediate vicinity of the ureteral orifice, however, may be removed as in another situation without much fear of injury to the ureter, care being taken to leave room enough when suturing the mucosa for the escape of urine from the ureter, as subsequently the latter reassumes its original appearance. Infiltrating growths situated about the ureteral orifice or on the anterolateral wall near the internal vesical opening require fairly extensive resection through the entire bladder wall, at least two centimeters beyond the affected area.

Infiltrating growths of questionable malignancy from a clinical standpoint, and necessitating the removal of considerable bladder area, may be removed after the method of Charles Mayo (*Annals of Surgery*, Vol XLVIII, p. 107): "The patient is placed in a high Trendelenberg position, and a median incision made from the pubes upward for 6 inches or more; the pelvis is well packed with gauze pads which hold the intestines in the upper abdomen. The abdominal incision is also protected by gauze pads. The bladder is caught up by two tenaculum forceps, lifted into the wound and opened by a 2-inch median incision. The small amount of fluid in the bladder is absorbed with gauze and the incision is enlarged upward and downward until it is ample for the purpose. The tumors may be cut from the bladder with scissors and the denuded area burned with cautery.

"The bladder wound, regardless of its size, is closed by a through and through continuous suture of catgut introduced in the original Connell method. This stitch is a running mattress suture and is passed through the entire thickness of the bladder wall, all loops passing from the mucous side, and when drawn close making a complete air-tight and water-tight continuous mattress stitch. The line of suture is now protected by a suture of silk, or preferably linen, applied as a Cushing parallel peritoneal suture, taking a square bite of the peritoneum first on one side then on the other of the line of closure, the needle being inserted parallel with the incision. This suture approximates the peritoneum and protects the primary suture just as when it is employed in gastro-jejunostomy, and is used for the closure of all the bladder incisions and resections, regardless of the amount removed."

Mayo further states in this same paper "That there are few lymphatics in the bladder, and these are exceedingly inactive, which fact delays metastases of malignancies, rendering them for a considerable period inactive, and that carcinoma of the bladder may, when taken early, be considered curable by operation.

Berg (see *American Medicine*, June, 1910), is rather pessimistic on the question of long postoperative duration without recurrence. Harris, in the *Annals of Surgery*, for October, 1902, claims that two-thirds or more of the bladder may be removed, and that the remainder will regenerate (?) (interrogation J. F. Erdmann's), and dilate to such a degree as to become a serviceable organ in many instances.

In view of the great number of intraperitoneal ruptures of the bladder operated upon, both by the general and the special surgeon, during the past twenty-five years, it appeared to the authors rather strange that the transperitoneal operation for the removal of bladder tumors had not been advocated years ago. Careful investigation of the literature, however, shows that Albarran in his "*Tumeurs de la vessie*," 1891, quotes Rydigier (*Wiener Medicinische Wochenschrift*, 1885), as advocating the deliberate transperitoneal resection of the organ, calling it laparocystectomy. (The authors have been unable to verify this reference.)

A great portion—one might say the majority—in single tumors of pedunculated papillomata surmount one or the other orifice. In seven cases of vesical neoplasms examined by us four were located about the left ureteral orifice, two about the right, and the most recent case involved the anterolateral wall just posterior to the ureteral orifice.

In such cases the possibility of injury to the ureter is always to be considered, and should the pedicle be infiltrated so that the growth is within a quarter of an inch of the ureter, the ureter should be excised at this point and a new implantation done. Where, however, the necessity of resecting a small bladder area with implantation of the ureteral orifice presents itself, this may be conducted extraperitoneally. It is desirable when possible to introduce a ureteral catheter to serve as a guide in locating the ureter as well as in its subsequent implantation.

In the extraperitoneal operation, having stripped the peritoneum laterally down to and beyond the ureter, one resects through the entire bladder wall, either from without inward or from within outward, as the case may be, employing the tumor mass and the ureter with its catheter as a pedicle. The bladder wall should be cut

in such a manner as to permit of proper closure of the wound. The ureter may then be implanted in that angle of the wound closely approximating its original situation, or it may be relocated by buttonholing the bladder wall, having in mind at all times the desirability of placing it as near its original position as possible, as well as the avoidance of kinking.

Immediately upon opening the bladder the entire vesical mucosa should be carefully searched for small outgrowths, which when found should be snipped with scissors and the stump cauterized before devoting our attention to the main growth. The necessity for such action arises from the fact that after exposure the mucosa becomes thrown into the folds which readily obscure small outgrowths, and which without removal would constitute a potential source of recurrence of the original condition.

Cystoscopic cauterization has been strongly advocated by Nitze, and the report of a few successful cases by Luys has been noted; while quite recently, intravesical treatment has been supplemented by Beers and Keyes of New York and others, who have practised fulguration or high-frequency currents in a few cases. This method, while showing considerable destructive action to the growths, is still in the experimental stage. It has, however, demonstrated in these cases its ability to bring about a cessation of hemorrhage in papillomata, something we have heretofore been unable to control. Of this method we will speak later.

In one case of carcinoma of the bladder coming under the observation of the junior contributor, Hodenpyle's serum was employed, but the patient reacted so unfavorably that its use was discontinued. Sarcomata or other neoplasms invading the bladder by extension from the prostrate may be treated by lumbar nephrostomy. In view, however, of the exceedingly great number of recurrences, and the almost invariably fatal nature of the condition, it would appear advisable to regard it as an inoperable one, and limit our interference to the employment of palliative measures.

It would appear, too that cystoscopic operative procedure should be limited to small, well pedunculated growths and the alleviation of hemorrhage in extensive recurrences; and that the best results are to be had from early diagnosis and wide removal either of the mucous membrane in the apparently benign type, or extensive resection of the entire bladder wall, either extra- or transperitoneally, with or without ureteral implantation, in the cases presenting indications of malignancy.

In three cases of well pedunculated growths seen and operated upon by J. F. Erdmann, one fairly small, one almost filling the bladder, and the third as large as an English walnut, the usual suprapubic operation was performed, and it was found in the progress of the cases that a small portable electric light and a Kelly proctoscope or Ferguson speculum were of decided benefit. The former allowed of free inspection of the bladder, while the latter was a useful contrivance during cauterization of the denuded area, preventing burning of the healthy bladder beyond the seat of involvement.

The bladder being opened and the growth outlined, a pair of Hunter or allied forceps were used to seize the pedicle, gentle traction was made so as to "cone" the mucous membrane and deeper walls of the bladder, then a curved forceps was used to seize the raised cone below its base. The growth was then excised and sutures of catgut placed below the clamp similar to the procedure in operating for hemorrhoids. The cautery was used within a Kelly proctoscope in one case for rather free bleeding from the upper angle of the wound. Guyon has devised a forceps for seizing the pedicle (see *Albarran,* 1909, p. 620), shaped somewhat like a sickle, that should work most satisfactorily in this type of removal.

Although I (J. F. E.) did not close the bladder in any of the three cases of pedunculated papilloma operated upon by me, I feel that I shall certainly do so in any subsequent noninfected cases. If we control hemorrhage at the time of removal of the growth, the use of a retention catheter for a couple of days, or an every three- to five-hour catheterization should be ample protection against leakage or rupture and infection, and would thereby diminish our patients' convalescence by weeks. A double-current catheter constant irrigation might also be an agent to promote prompt repair.

In my second case, a papilloma the size of an English walnut, a very disagreeable pelvic and saphenous phlebitis complicated an otherwise slow convalescence.

Case I—Service of J. F. Erdmann. E. F., 42 years of age, was operated upon on October 30, 1905, previous to which time he gave a history of repeated vesical obstruction, with voiding of blood and bloody urine. The obstruction, which was of a temporary nature, was usually relieved by the passing of a sound. When seen by me he had just experienced an attack of this sort in the South. The character of the obstruction was somewhat similar to that of stone. The stream would shut off suddenly, but without pain, and all the straining possible would fail to release the obstruc-

tion. At the time of the attack in the South a small white fragment was passed, which he preserved and brought with him. On gross appearance it resembled a fragment of papilloma. Microscopic examination demonstrated it to be of papillomatous material. Cystoscopy a couple of days later showed a papillomatous growth on the outer side of the orifice of the left ureter.

The operation was done supapubically. The growth was about as large as a chestnut, and the small pedicle was clamped off and treated as described above. Upon releasing the clamp after tying the suture I found rather free spurting of blood from the upper angle of the wound. A Kelly proctoscope was introduced, so as to enclose the area operated upon, and with the aid of a small electric light the bleeding point was rapidly sponged and effectively touched with the actual cautery. The patient was discharged in sixteen days.

Case II—Service of J. F. Erdmann. H. F., 40 years of age, visited me in September, 1907, and gave a history of occasional bleeding in a very short period of time. The urine varied from a slight evidence by microscope to very profound evidence of fresh and disintegrated blood. On his second visit to me in the office he passed urine the color of coffee, filled with sediment. There were no evidences of pain whatever at any time in his history, his attention being called to the trouble by seeing the discoloration of the urine. Cystoscopy showed a papilloma about the size or a filbert, near the right ureteral orifice, and pedunculated. This was removed September 23, 1907, and, barring a phlebitis, both pelvic and saphenous; his convalescence was without further note, the wound in the bladder having healed in fourteen to sixteen days. The method of removal was suprapubic. The pedicle was grasped in the forceps and excised through the mucosa and submusoca, with final suture.

Case III—Service of J. F. Erdmann. A. C. M., about 30 years of age, came to me November 27, 1906. Eighteen months before, while urinating, he noticed that he was passing blood, and that at certain times it would be almost pure blood. Then there were evidences of intermittent bleeding, sometimes just enough to stain the urine, sometimes profound discoloration with clots. There would occasionally be a spasm upon urinating, before the bladder was empty. In the past two months there had been no visible evidences of blood until one week before his visit, when he observed fairly profound evidences again. Bloody urine would be induced by jumping on and off cars. He had never had any pain referable to kidneys, perineum, bladder, or urethra, and no thigh or leg pains. Health otherwise was absolutely perfect. Once he had slight pain in his groin; occasionally has had pain in the lower right side. Has never had any specific disease. He said that the first voiding of blood occurred subsequent to taking a bottle of citrate of magnesia, which was followed by violent catharsis. Urine analysis was negative as to kidney cells, casts, and the like. He had never had any putrid urine, nor been examined by cystoscope or searchers. There had been no loss of flesh. He voided an ample quantity of urine. Cystoscopy showed papilloma of very large size, which apparently arose from the left side.

Suprapubic operation was done on Thanksgiving Day, 1906. Upon exposing the interior of the bladder it was found that the papilloma arose from a base of 1½ inches in length and ¼-inch in width, just above and to the left of the left ureteral orifice. The papilloma itself was one that practically filled the hand. Removal was made by means of excision and suture of the gap in the mucosa. The patient made a recovery in a period of three to four weeks.

Case IV—Service of J. F. Erdmann. This was a case sent me for diagnosis through the courtesy of Dr. Pomeroy, of Waterbury, Conn., and gave the following history: P. L., 36 years of age. Gonorrhea three years ago, and bloody urine off and on for ten years. Has had no pain, no lump, and no weakness except from bleeding. Goes for a period of time with no bleeding, then will have bloody urine for three or four weeks. Has passed clots. Examination by cystoscope showed a beautiful large papilloma to the left. I herewith append a letter from Dr. Pomeroy, following the operation:

"I have been waiting for the pathologist's report before answering your letter regarding the case of P. L. I took him into my service at the Hospital and we operated on him February 14. I found a single papilloma near the left ureteral opening, pedunculated, and about the size of a mandarin orange. The pathological examination did not show any evidence of malignancy. The pedicle showed no cell infiltration of either epithelial or connective-tissue types. The patient made an uneventful recovery, and was discharged cured March 5."

Case V—Service of J. F. Erdmann. J. K., 55 years of age, has had bladder difficulties for a number of years, voiding three to five times at night and every half-hour or oftener during the day. Pain on riding, similar to that manifested by stone in the bladder; stream has been known to shut off; passes blood occasionally; is not certain,

but thinks he has lost flesh. Examination by cystoscope showed no evidences of stone, but a large tumor, pedunculated, and about 2 inches long, 1½ inches wide, and 1 inch deep, was found situated on the fundus, slightly to the left of the median line, covered over its greater area with a calcareous deposit. This deposit was felt by his family physician, who sent him to me for a stone in the bladder. Operation, suprapubic transvesical. Analysis proved the growth to be epithelioma.

This operation was done on July 22, 1910, and, although rather early to include in a paper, he presented such a marked improvement in symptomatology that I feel the case is worthy to be reported.

In addition to these cases two malignancies of the bladder in females have occurred in my service; one in a woman of forty-seven, in whom the tumor was a typical carcinoma and situated in the left ureteral zone. Her history is as follows:

Case VI—Service of J. F. Erdmann. I saw this patient ten years ago, with a large tumor involving the left area of the bladder wall, in the vicinity of the ureteral orifice. The growth was so advanced that it was impossible to state whether or not this tumor had been a papilloma with malignant degeneration. No operation.

Case VII.—Service of J. F. Erdmann. Miss H., 44 years of age, the second of the female patients mentioned above, came to me in September, 1908. She had been perfectly well up to two years before this time. She first noticed bloody urine at the urethra, and was operated upon for urethral caruncle. She had a cessation of menses for one year, then a recurrence. From June to September she had passed blood daily. The voiding of urine with blood has always been painful. Some loss of flesh. The external meatus was negative, but the floor of the urethra near the internal meatus was enlarged to about the size of the thumb, and continuous with a large mass in the left portion of the bladder. No uterine invasion. She returned in December, having refused operation at the previous visit. At this time I did a suprapubic section, and found that the growth involved over 50 per cent. of the bladder capacity. Dr. Brooks of Carnegie Laboratory reported the analysis as follows.

"The growth is a carcinoma of the encephaloid variety. In so far as one is permitted to judge from the histological structure and especially from the type of the cells and their arrangement, one would think that the growth was most likely to have originated from the mucous membrane of the bladder. This is the youngest case of primary cancer of the bladder that I have ever seen in a woman."

Dr. Brooks further remarks that in his experience primary malignant tumors of the female bladder are quite rare, and in this I agree with him, having seen but the two cases here recorded. I concluded this operation by simply removing the section, and establishing for the patient's comfort a suprapubic drainage. She died in February, 1909.

Since writing the above portion of this paper, which was to have been presented before the Genitourinary Section of the New York Academy of Medicine last spring, cases numbers one and two have returned with histories of blood showing in the urine.

Case I, upon cystoscopy showed a large mass, suspicious of malignancy, to the left of his bladder near the ureteral orifice; while Case II shows upon cystoscopy four papilomata that to all visual signs are benign.

These two cases I have turned over to Dr. McCarthy for experimental fulguration. His citation is appended below, with reports of three other cases.

Case VIII—Service of J. F. McCarthy. Male, 65 years of age, admitted to Bellevue Hospital two and a half years ago. Hematuria for six months, spontaneous. At the time of admission he was in a state of uræmic coma which lasted about three days, after which time his condition improved. At this time his bladder capacity was 3 drams. Following three months' observation and treatment his capacity was brought up to 16 ounces, and cystoscopic examination showed cauliflower growth over the right ureteral orifice, probably malignant. Operation refused, and observation continued to date.

Observations—Bladder lavage in this case, contrary to the general belief, brought about marked improvement, and while its effect on the hematuria was little if any, none the less greatly increases the bladder capacity, and the patient has gained 20 pounds during this time. Creolin was found to be the best in lavage.

Case IX—Service of J. F. McCarthy. Italian, 40 years of age, hematuria intermittent in type lasting one year. One interval of six months with absence of macroscopic blood. Cystoscopic examination revealed cauliflower growth totally obscuring the left ureteral orifice.

Operation—The bladder was opened, and a large infiltrating growth involving the base and lateral walls, and including the ureter, on that side, was found. It was deemed advisable simply to remove a section for microscopic examination. The report

was a gland-cell carcinoma. The wound apparently healed, but within three months, during which time the growth increased to immense proportions, the patient died. Before leaving the hospital, however, he was subjected to several injections of Hodenpyle serum, but he reacted violently after each injection, and with no apparent beneficial result.

Observations—Contrary to the usual custom this neoplasm in a short time underwent a very marked increase in size.

Case X—Service of J. F. McCarthy. Coachman, 56 years of age, well preserved. Hematuria for six months. Cystoscopy showed a well marked cauliflower growth obstructing the left ureteral orifice, and a widespread condition greatly resembling a bullous edema.

Operation—The bladder was opened, the growth grasped with a Guyon tumor clamp and cauterized with actual cautery to its base. Upon release of the clamp a well defined gush of urine escaped from the middle of the mass. Following the operation the hematuria disappeared, and since that time, a period of four months intervening, the patient has enjoyed apparent good health. Subsequent cystoscopy shows the abeve-mentioned edema as persisting, and a well marked cicatrix at the site of the tumor.

Observations—Unusual feature of well defined bullous edema; also the fact that active cauterization which must have involved the ureteral mouth has had no subsequent ill effect on the latter. (See Albarran.)

Dr. McCarthy's report on Case I: recurrent after nearly five years. One large villous growth situated just behind the left ureteral orifice. Three fulguration treatments with marked diminution in size.

Remarks: fact of recurrence at a site remote from the position of the original growth.

Dr. McCarthy's report on Case II: recurrent papilloma after nearly three years. Four small papillomatous outgrowths at the site of probable incision in the roof of the bladder, and one larger similar mass on the left lateral wall. Three fulgurations with the Oudin current, with hematuria absolutely stopped, and considerable diminution in the size of the growths.

Remarks: marked effect on the hematuria, which may be brought about by no other agent.

As to Fulguration—I find the technic incomparably more difficult than ureteral catheterization, and consider that the procedure should be confined to those expert in cystoscopic operation. Of course the work done along this line is at present in so immature and incomplete a state that one should be exceedingly conservative in anticipating results. That it does, however, bring about a cessation of the hematuria in the vast majority of cases there can be little doubt, and this in itself is a distinct gain. It is also a well-known fact that this agent will destroy similar growths on the skin surface of the body, and it would seem that the water medium customarily employed may ultimately be dispensed with in favor of air dilatation, and in this way it is my opinion that a much more rapid and profound action may be anticipated. In my work in intravesical fulguration I have found it essential to have absolute control of the make and break of the current, and to this end I have had constructed for me by Mr. R. Wappler a foot switch that operates most successfully.

Certain situations of these neoplasms, such as in the case mentioned where four papillomata are located in a straight line on the median aspect of the vault of the bladder, may be found difficult of approach. The difficulty in this case has been readily overcome by pressure of the hand on the hypogastric region above. No prostatic malignancies, nor those in which the question of secondary invasions of the bladder arose are considered in this paper.

Physical Examination—The rectal or vaginal examination should never be omitted in these cases. Catheterism is not of much value and is dangerous on account of hemorrhage and cystitis. The course of the condition is generally long, twelve to fifteen years. The frequency and abundance of hematuria, of course, plays the great rôle in duration. Death may at times take place from obstruction of the mouth of the ureter, provoking hydronephrosis or anuria, or a reflex anuria may supervene. Finally, the tumor may recur as a malignant one.

Recurrences as Malignancies—Certain authors base their claims that the malignant tumors undergo their evolution on the spot, as they cannot be spread by means of lymphatics, there being none (?) in the bladder. This theory is based on the researches of Professor Sappey, who denies the existence of lymphatic vessels in the bladder coats. This idea has, however, been controverted by the work of M. and Mme. Hoggan, who have proved the existence of these vessels in the bladder. Other authors have claimed that these growths are in reality in their incipiency benign tumors, and at a given moment become transformed into malignant ones.

Mortality—Francis S. Watson (*Annals of Surgery*, December, 1905, *Operative Treatment of Tumors of the Bladder*), says "The sum and substance of the result of operative treatment to the present time may be stated thus: if the operative deaths and rapid recurrences are combined under the head of 'operative failures,' such failures are seen to have occurred in 28.6 per cent. of cases in benign tumors, exclusive of myoma, and in 46 per cent. of cases of carcinoma."

According to the same author, out of 653 cases of all tumors operated upon, 243 were benign and 410 malignant. That the benign tumors recurred rapidly in 20.5 per cent., the carcinomatous in 26.8 per cent., and the sarcomatous in two to eight months in all except two out of fifty-two cases.

Conclusions—That tumors of the bladder are translatable by the symptomatic hematuria and other symptoms, which do not always permit clinically of a striking difference between them, inasmuch as a small papilloma may give rise to a fatal hematuria as well as a malignant one, seems established. However, one may arrive in certain cases at a precise diagnosis based upon the clinical evolution, the physical signs, and the examination of the fragments expelled. That the benign tumors may recur under two forms, first under the malignant form, a long period of time intervening before the recurrence; and it is a question whether the tumor beginning as a benign one has not become transformed into a malignant one. The actual state of our knowledge of the subject does not at this time permit of this conclusion. Second, a recurrence may take place after a long period of time as a benign one, as in two cases recorded by me with histological findings.

Guyon states that "the cases which I believe have permitted of this hypothesis of a transformation are very exceptional. I have already had an occasion to cite in studying the progress of neoplastic affections of the bladder many examples of vesical tumors of long duration, even up to twenty-seven years, which did not undergo malignant transformation. Consequently one should be very reserved in discussing the question of transformation of vesical growths."

ORIGINAL COMMUNICATION.

PROLAPSE OF THE UTERUS.

Report of the Results of One Year's Work, in Ward 23, Dr. W. M. Polk, Visiting Gynaecologist, in the Correction of Uterine Prolapse and Posterior Displacements.

George Dempster Hamlen, M.D.

(*Adjunct Assistant Gynaecologist.*)

The appended classifications show the nature of the diseases, the operations employed for the relief of the conditions found and the results as far as obtainable up to the present time.

In January, 1909, Dr. Polk performed an operation for prolapse of the uterus, using a method which he has devised for strengthening the upper pelvic floor. Later he made use of this same procedure in cases of retroversion of the uterus, both with and without adhesions where the prolapse was less marked.

During the past year (October, 1909, to October, 1910), all cases of prolapse have been treated by his method, and the results have been most satisfactory. All seven cases have reported during the present month.

Dr. Polk's operation, like others employed for the purpose of restoring the uterus to its normal position, aims to strengthen the upper pelvic floor at the base of the bladder and around the utero-vaginal junction.

It differs from other operations in that the approach is made by the suprapubic route. A full description is found in the Transactions of the American Gynæcological Society, 1909

In short the steps of the operation are, to open the abdomen, Trendelenburg posture, grasp the fundus of the uterus and while traction is made upon it, separate the bladder from the upper part of the vagina through an incision made antero-posteriorly just at the attachment of the bladder to the uterus. Ligatures of kangaroo tendon are then passed, catching the lateral portions of the vagina quite up to broad ligament including basic lines, which have been exposed and approximating them in the

median line. The excess of peritoneum is folded in in closing the peritoneal incision. The position of the uterus is further sustained by shortening the utero-sacral ligaments.* The abdominal incision is then closed and the lower pelvic floor repaired by perioneorrhaphy.

No patient has had a return of diseased condition. In two cases the operation was performed over a year ago and in four cases six months have passed. One of the last four is pregnant at four months.

These results without a failure up to the present time show that the operation is one selection for cases of prolapse of the uterus.

Retroversion of the Uterus.

Of the numerous operations for retroversion of the uterus and its accompanying conditions five have been made use of:

1. Dr. Polk's operation.
2. Alexander operation.
3. Alexander operation through Pfannenstiel's incision.
4. Internal shortening round ligaments.
5. Goffe's operation.

Dr. Polk's operation has been used in seven cases of retroversion uterus; three without adhesion and three when adhesions were present with the displacement. In one case only was the result unsatisfactory. Three of the seven cases have reported for examination. One is now seven months' pregnant.

For retroversion the operation does not require separation of the bladder. Merely approximation of lateral vaginal wall above bladder and in some cases the round ligaments are in addition shortened.

Alexander's operation was selected as the proper one in eleven cases. These were those where the upper pelvic floor was not weakened to any marked extent, where the bringing of the uterus into its normal position with repair of the lower pelvic floor where necessary.

An operation which will restore the uterus to its normal position, with little shock to the patient, with the probability of permanent relief without danger of complications in subsequent pregnancies is an ideal one. This is found in the Alexander operation in selected cases. The unsuccessful results reported elsewhere have been the result in the majority of instances of wrong diagnoses. The operation should never be employed if there is any possibility of adhesions being present or in inflammatory conditions of the appendages. A prolapsed ovary which does not return to its normal position following the reposition of the uterus should also militate against the use of the Alexander operation.

Objections have been urged by numerous operators who claim that there is great difficulty in finding the ligament and that often when found and traction is made upon it, it is very liable to rupture. These objections should not be used against it, however, for with the proper anatomical knowledge and the requisite surgical skill both objections are met and overcome. The ligament is occasionally broken, but under these circumstances the inguinal ring can be slit up and the broken end, which is usually larger as it gets nearer the uterus, caught.

Given then a retroverted uterus without adhesions and without prolapse or inflamed adnexa, Alexander's operation has given excellent results.

It has been possible to examine only three of these cases during this month. The position of the uterus was found normal in these three.

One of these, K. M., confined since her operation. Her labor was difficult, necessitating the use of bags to dilate the cervix. She was told that her difficult labor was due to her operation, but her history shows that her two previous labors were equally difficult and as she was perfectly well during her pregnancy, having no symptoms up to the time of her labor, her dystocia can hardly be attributed to the Alexander operation.

When the uterus is retroverted and adherent or the uterus displaced posteriorly and the appendages diseased, naturally some operation must be employed which will permit us to reach the site of the affected structures. The success of the conservative work upon the appendages will often depend upon the ability to keep a uterus in an anterior position following such conservative work. Many patients upon whom con-

* Recently this has been in one case successfully done by drawing a loop of this ligament through the lower inner angle of broad ligament—perforated for this purpose—and stitching it to side of utero-vaginal junction in front of broad ligament. The sacral ligaments were in this case very loose and elongated. Injury to the utero-vaginal plexus is thus avoided.

PROLAPSUS UTERI—Dr. Polk's Operation.

Name.	Age.	Civil State.	Operated.	Diagnosis.	Operation.	Discharged.	Result.
L. V.	35	Married.....	Nov. 15 Dr. Polk	Prolapsus uteri	Dr. Polk's	Jan. 13	Examination Dec. 7, 1910. Uterus in good position. Occasional slight pain in region of broad ligament. No induration.
M. D.	38	Married.....	April 29 Dr. Polk	Prolapsus uteri with adhesions and chr. salpingitis	Dr. Polk's	June 28	Examination Dec. 5, 1910. Uterus in normal position. Feels perfectly well.
E. H.	48	Widow.....	May 19 Dr. Polk	Prolapsus uteri, cystocele, rectocele, lac. perineum	Dr. Polk's	Aug. 10	Dec. 8, 1910. Reported by letter. Feeling well and able to do work as usual. No return of trouble.
M. W.	42	Widow.....	May 27 Dr. Polk	Prolapsus uteri	Dr. Polk's	June 23	Examination Dec. 5, 1910. Uterus in normal position. Slight cystocele. Feels perfectly well.
B. R.	26	Married.....	June 3 Dr. Polk	Prolapsus uteri, retroverted and adherent	Dr. Polk's	June 24	Examination Dec. 8, 1910. Feels well. Is four months pregnant.
M. D.	42	Married.....	Sept. 30 Dr Polk	Prolapsus uteri, cystocele and rectocele, ventral hernia	Dr. Polk's	Oct. 30	Examination Dec. 8, 1910. Uterus normal position. Slight rectocele, increased during defecation.
M. M.	50	Widow.....	Nov. 22 Dr. Polk	Prolapsus of stump of cervix, cystocele and rectocele	Dr. Polk's	Feb. 10	Examination Dec. 8, 1910. Excellent result. No prolapse of vaginal wall.

RETROVERSION UTERI—Dr. Polk's Operation.

Name.	Age.	Civil State.	Operated.	Diagnosis.	Operation	Discharged.	Result.
T. K.	35	Married.....	Jan. 14 Dr. Polk	Retroversion uteri with adhesions	Dr. Polk's	Feb. 5	Examination Dec. 5. Uterus in normal position. Patient feels well. Slight increase of urination.
M. MacI.	26	Married.....	Feb. 18 Dr. Polk	Retroversion uteri with adhesions	Dr. Polk's	Mar. 10	Uterus in good position; no tenderness; slight thickening of broad ligaments.
M. B.	40	Married.....	Jan. 31 Dr. Polk	Retroversion uteri	Dr. Polk's	Feb. 23	Examination Dec. 5. Has felt perfectly well since operation. Now 7 months pregnant.
E. C.	25	Married.....	Jan. 31 Dr. Polk	Retroversion uteri	Dr. Polk's	Feb. 23	Examination Dec. 7. Does not feel well and has not since operation. Uterus retroverted and apparently adherent; tender. Painful copulation and defecation.
A. C.	28	Married.....	Mar. 4 Dr. Barrows	Retroversion uteri	Dr. Polk's	Mar. 23	Uterus in good position when discharged.
M. D.	24	Married.....	April 1 Dr. Barrows	Retroversion uteri with adhesions	Dr. Polk's	April 22	Three weeks after operation uterus in good position. Some exudate and tenderness behind.
B. F.	25	Single.....	April 11 Dr. Polk	Retroversion uteri with adhesions	Dr. Polk's	May 10	Cured.

RETROVERSION UTERI, NON-ADHERENT—ALEXANDER OPERATION.

Name.	Age.	Civil State.	Operated.	Diagnosis.	Operation.	Discharged.	Result.
A. L.	37	Married.....	Oct. 12 Dr. Barrows	Retroversion uteri, lac. cervix and perineum	Alexander	Oct. 27	Cured.
M. K.	27	Widow.....	Oct. 1 Dr. Barrows	Retroversion, lac. cervix, chr. endo-metritis	Alexander Curettage, trachelorrhaphy	Oct. 12	Examined Dec. 5, 1910. Uterus in normal position. Patient well.
A. K.	21	Married.....	Oct. 18 Staff	Retroversion uteri	Alexander	Nov. 3	Cured.
E. G.	49	Married.....	Oct. 19 Dr. Barrows	Retroversion uteri, endo, lac. cervix and perineum	Alexander Curettage, trachelorrhaphy and perineorrhaphy	Nov. 12	Cured.
C. R.	24	Married.....	Oct. 19 Staff	Retroversion uteri, endo-metritis	Alexander Curettage	Nov. 3	Cured.
M. P.	28	Married.....	Nov. 12 Dr. Polk	Retroversion uteri	Alexander	Dec. 5	Cured.
K. M.	23	Married.....	Feb. 1 Dr. Barrows	Retroversion uteri, cystocele and rectocele	Alexander Trachelorrhaphy and perineorrhaphy		Well up to birth of child 2 months ago. Uterus in good position. Slight hernia right of left scar following labor. Examined Dec. 5.
D. S.	24	Married.....	Mar. 22 Dr. Barrows	Retroversion uteri	Alexander	April 19	Cured.
C. Y.	25	Married.....	June 7 Staff	Retroversion uteri	Alexander	June 28	Cured.
M. S.	22	Widow.....	July 12 Dr. Barrows	Retroversion uteri, endo, lac. cervix	Alexander Trachelorrhaphy	Aug. 5	Cured.
H. L.	24	Single.....	July 18 Dr. Barrows	Retroversion uteri, chr. endo-metritis	Alexander Curettage	Aug. 2	Reported Dec. 7. Perfect health No symptoms.

RETROVERSION UTERI, PFANNENSTIEL'S INCISION WITH ALEXANDER.

Name.	Age.	Civil State.	Operated.	Diagnosis.	Operation.	Discharged.	Result.
H. H.	35	Married.....	Nov. 23 Dr. Barrows	Retroversion uteri	Combined Alexander	Dec. 9	Examined Dec. 9. Uterus in position. No symptoms.
G. G.	30	Married.....	Mar. 18 Dr. Barrows	Retroversion uteri, adherent previous laparotomy	Combined Alexander		Examined Dec. 7. Uterus in normal position. Occasional pain in lower abdomen.
E. H.	43	Married.....	Mar. 22 Dr. Barrows	Retroversion, adhesions	Combined Alexander		
M. G.	35	Married.....	April 26 Dr. Barrows	Retroversion uteri, adherent endo-metritis, lac. cervix and perineum	Combined Alexander	May 1	Cured.
M. R.	23	Married.....	May 3 Staff	Retroversion, adhesions, chr. ovaritis	Combined Alexander	June 9	Examined Dec. 7, 1910. Uterus in normal position. Feels perfectly well.
M. K.	40	Married.....	June 20 Staff	Retroversion uteri, adherent	Combined Alexander	July 16	Cured.
H. L.	24	Married.....	June 22 Staff	Retroversion uteri, adherent	Combined Alexander	July 16	Examined Dec. 5, 1910. Uterus normal. Feels perfectly well.
E. F.	23	Married.....	Jan. 25 Dr. Barrows	Retroversion uteri, adhesions, cystic	Combined Alexander		Cured.
M. F.	34	Single.....	Mar. 18 Dr. Barrows	Retroversion uteri, ovary adhesions	Penn Combined Alexander	April 3	Cured.

RETROVERSION UTERI (INTERNAL SHORTENING)

Name.	Age.	Civil State.	Operated.	Diagnosis.	Operation.	Discharged.	Result.
A. J.	17	Single.....	Oct. 15 Staff	Retroversion uteri, prolapse ovaries, adhesions	Internal shortening, round ligs., plastic left ovary	Nov. 1	Cured.
C. D.	39	Single.....	Nov. 23 Dr. Barrows	Retroversion uteri	Internal shortening, round ligs.	Dec. 13	Cured.
J. M.	26	Married.....	May 6 Staff	Retroversion uteri, chr. endo-metritis	Internal shortening, round ligs.	May 23	Cured.
K. D.	32	Widow.....	May 24 Staff	Retroversion uteri, adherent cyst right ovary	Internal shortening, round ligs., right salpingo-oöphorectomy	June 13	Cured.
F. B.	50	Married.....	May 27 Staff	Retroversion uteri, adherent abscess right ovary, ventral hernia	Internal shortening, round ligs.	June 23	Examination Dec. 9. Uterus in good position. No symptoms.
M. S.	24	Married.....	Aug. 9 Dr. Hamlen	Retroversion uteri, adherent chr. salpingitis	Internal shortening, round ligs., left salpingo-oöphorectomy	Aug. 22	Cured.
S. E.	18	Single.....	Sept. 12 Staff	Retroversion uteri, double salpingitis	Internal shortening, round ligs.	Sept. 28	Reported Dec. 11. Feels perfectly well.
E. B.	24	Single.....	July 8 Dr. Hamlen	Retroversion uteri, lac. cervix and perineum	Internal shortening, round ligs.	Aug. 1	Cured.

RETROVERSION CYSTOCELE—Goffe Operation.

Name.	Age.	Civil State.	Operated.	Diagnosis.	Operation	Discharged.	Result.
W. E.	14	Single.....	June 24 Dr. Hamlen	Retroversion uteri, cystocele, lac. perineum	Goffe	July 14	Cured.
E. C.	23	Married.....	July 26 Dr. Hamlen	Retroversion uteri, cystocele, lac. perineum	Goffe	Aug. 12	Examination Dec. 7. Uterus in normal position. Feels perfectly well.

servative work has been done have failed to obtain relief and the result counted against conservative operations because the uterus has not been properly secured.

On account of this, almost every case of conservative work is accompanied by some measure to hold the uterus forward and so prevent as far as possible the reformation of adhesions. Two operations have been made use of for this purpose:

1. The Alexander operation when the Pfannenstiel's incision has been used (combined Alexander operation).

2. The shortening of the round ligaments somewhat after the method of Wylie, when the median incision has been employed.

The number of cases treated by these methods has been about equal and the results equally satisfactory.

Ventral suspension or fixation has not been used owing to the unsatisfactory results and the great danger to patients should pregnancy follow.

Internal shortening has the advantage in that the operation takes only a few minutes, but is open to the objection that the strongest part of the ligament is shortening, while the weaker portion where it enters the internal ring is not strengthened and the ligament has been known to have elongated at this point. To a great extent this objection may be overcome if the end of the loop taken in the ligament is fastened to the peritoneum just at the internal ring.

Four cases of the combined Alexander and two of the internal shortening reported. In all the uterus was in normal position.

Two cases with marked cystocele and only slight prolapse and retrodisplacement of the uterus were operated on by the Goffe method. One has reported during this month. The result satisfactory. Uterus normal position, no cystocele.

THE OPERATIVE TREATMENT OF PELVIC INFECTION.*

George H. Mallett, M.D.

All who have practised gynecology for the last fifteen or twenty years must review with interest the changes in the method of treating pelvic infections. Before asepsis and improved technic permitted the abdominal cavity to be opened with impunity, palliative measures and local applications of iodine and glycerine tampons were the sole means of relief. Then came the operative methods. When in most cases it was found that the tubes and ovaries were diseased, or were thought to be, then came immediate laparotomies, performed during the acute stage of the disease, and followed by a ruthless sacrifice of organs and a high rate of mortality. A considerable number of these patients, suffering from suppurative diseases who survived the removal of their appendages, still were not relieved until the whole uterus was also removed. The rule was then formulated that when the tubes and ovaries were removed, the "emasculated" uterus should also be taken out. This rule is observed by many operators to-day. Then the pendulum swung the other way and so-called conservative surgery took the place of radicalism and while many tubes and ovaries were saved, others were allowed to remain in such a diseased condition that a subsequent operation was required for their removal.

Have we at the present time attained all that could be desired in the treatment of these diseases? No, but better judgment is being used in deciding when to operate and what tissues shall be removed and what shall be allowed to remain; and the improvement has been very marked, both in the greatly reduced mortality and in the ultimate results. This is shown by the mortality records and by the diminished number of postoperative patients at the hospitals and clinics.

The object of this communication is to recall or emphasize some measures that may be used against pelvic infection to check its progress and to treat the diseased organs and tissues in such a way that they may recover their usefulness.

By pelvic infection is meant an inflammation of the endometrium, the uterus, the tubes, the ovaries, and the cellular tissue of the pelvis, caused by bacteria. Part of the pelvic organs or all may be involved in the inflammation.

Pelvic infection is the most important of all gynecological diseases and causes most of the sufferings in gynecological patients, and more deaths than all other gynecological diseases combined, and operations for its relief are more dangerous than for other gynecological conditions.

* Reprinted from the American Journal of Obstetrics, Vol. LX, No. 2, 1909.

The microorganisms most commonly found in pelvic infections are the gonococcus, streptococcus pyogenes, staphylcoccus pyogenes albus, citreus, and aureus, colon bacillus, tubercle bacillus.

Among the rarer organisms found are the micrococcus lanceolatus, the bacillus lactis aerogenes, and the proteus zenkeri. A very complete list of the bacteria that infect the pelvis and their relative frequency is given by Andrews (Amer Jour, Obst., vol. xlix, No. 2) in his report of bacteriological findings in forty-two cases of pyosalpinx, and in the carefully conducted investigations at Johns Hopkins Hospital the results of the cultures taken from infected ovaries and tubes and from the endometrium, coincided with those obtained by him.

A mixed infection may occur, consisting of the streptococcus and staphylococcus albus and aureus or the colon bacillus. From the writings of Schwartz, Noeggerath, Sanger, and Zweifel, as well as the reports from American authors, it is a conservative estimate to say that 50 per cent. of all infections of the genital tract are caused by the gonococcus. As pregnant women are infected with gonorrhea in many cases, a certain number of puerperal infections are caused by this gonococcus. Next to the urethra, the uterus is most frequently infected with gonorrhea, either directly or from the infected vaginal discharges. This bacterium infects the previously healthy and uninjured mucous membrane and almost always travels by extension into the tubes. There its progress may be arrested by a reactionary inflammation and the disease limited, or it may escape into the pelvic peritoneum and set up a localized peritonitis.

Although the gonococcus is usually confined to mucous membrane, it has been found in the uterine tissue and has caused a general peritonitis and at other times has entered the general circulation and caused arthritis and endocarditis.

In mucous membrane the gonococcus lives indefinitely, while in an abscess cavity it readily dies.

The symptoms of infection of the uterine cavity are usually preceded by those of infection of the urethra, vagina, Bartholin glands, etc. The chief symptoms referable to the endometritis are leukorrhea, pain, a feeling of weight in the pelvis, elevation of temperature and its accompanying discomforts, and irregular menstruation. These vary in proportion to the virulence of the infection and the extent of tissue involved.

Palpation shows the uterus to be slightly enlarged and very tender. After the disease becomes chronic the only marked symptoms to remain are the leukorrhea and the frequent and prolonged and painful menstruation.

In from 30 to 50 per cent. of the cases of gonorrhea the tubes and ovaries are infected. The extension may occur in several days or several months after the primary infection. The onset is marked by acute pain in the ovarian region, slight fever, painful micturition and defecation. When pus forms the patient may have chills and moderate febrile reaction.

The infection that follows labor or miscarriage or operative procedures, the introduction of instruments, intrauterine applications, etc., is usually caused by the streptococcus pyogenes, although the staphylococcus, colon bacillus, and saprophytic bacteria have been found. The same bacteria that are found in wound infection in other parts of the body are found in septic endometritis and pelvic infections.

When infection occurs from the streptococcus the local changes are slight. These bacteria penetrate the uterine wall, spread rapidly by the lymphatics or blood-vessels or by the blood circulation, and rarely by the tubes, in contrast to the mode of extension of the gonococcus. Mascagni and Poirier have shown that the uterus and its appendages, as well as the vagina, is surrounded by a dense network of lymphatics, and that the upper part of the vagina and around the cervix is more richly supplied with these vessels than the other portions of the genital tract, for here the lymphatics collect before entering the glands of the pelvic floor. The lymph-vessels of the body of the uterus either pass out through the mesosalpinx, near the ovarian attachment and up the suspensory ligament of the ovary to the lumbar glands or course down the round ligaments to the deep inguinal glands.

These lymphatics lie with the blood-vessels in the cellular tissue of the pelvis. The extent of the pelvic celluar tissue and its importance, pathologically, is clearly shown by A. von Rosthorn in the beautiful illustrations accompanying his paper, "Krankheiten des Beckenbindegewebes" (Handbuch der Gynäkologie, 1899).

The infection of the streptococcus, whether it results in exudates or abscesses, is usually asymmetrical, differing thus from the gonococcus.

When the streptococcus is mixed with the colon bacillus or staphylococcus there is greater local reaction than in the pure infection. The symptoms usually begin with a chill and elevation of temperature varying with the severity of the attack and generally ranging from 102° to 104° and pulse from 110 to 120. Pain is usually not

great until the peritoneum or periuterine tissue becomes involved, and then it is usually severe. The patient feels ill and the prostration is marked.

The uterus is larger, more doughy and tender than normal. If the infection is limited to the uterine cavity the temperature gradually falls and the symptoms subside and the uterus becomes normal; usually, however, a chronic endometritis is left.

If the infection has extended beyond the uterus, then the symptoms become those of the parts infected, as peritonitis, lymphangitis, etc.

With streptococcus infection there is little leukorrhea and no odor. When the odor is present it is due to mixed infection, usually the colon bacillus. The diagnosis can be made from the history, the general condition of the patient, and by bacterial examinations. In chronic cases the history is of still more importance in determining whether the infection has been of gonorrheal or streptococcic origin.

The gonorrheal almost always extends along the mucous membrane, causing purulent tubal inflammations or peritoneal abscesses, generally bilateral.

The streptococcoccic follows pregnancy, uterine traumatism, etc., and extends through the lymphatics, does not cause pus tubes as a rule, and is asymmetrical.

In discussing the operative treatment of pelvic infection, it is not my intention to consider prophylaxis nor palliative measures; not from a lack of appreciation of the importance of these measures, but from lack of space. Since it is a matter of common observation that a certain proportion of cases of pelvic infection recover spontaneously, all means should be used to bring about this happy termination. Should the case be one of gonorrheal endometritis, our efforts should be directed toward limiting the disease to that tissue and preventing its invasion of the tubes. The means to be employed are the so-called palliative, and consist of the recumbent position, ice-bag or hot-water bag to lower abdomen, hot vaginal douches, liquid diet, saline cathartics, and opiates when needed. Should suppuration reach the tubes notwithstanding our efforts, the same palliative means may be used until resolution occurs or a pyosalpinx forms. If resolution does not occur the case becomes an operative one. If the diseased structures are to be attacked through the abdominal route, then the operation should be delayed until the case becomes chronic and the pus sterile, as indicated by the temperature. A disregard of this rule was the cause of the high mortality in these cases in former years.

The writer believes the best way to treat this condition—tubal infection—is by vaginal section and drainage, for this can be done with safety during the acute stage and the necessity for waiting until the tubes and ovaries are distended with pus and damaged almost beyond repair, can be avoided.

As soon as any induration is felt in the floor of the pelvis or the tubes and ovaries are found to be enlarged and tender, a vaginal section should be made, regardless of the temperature. The tubes are carefully examined and the os abdominalis opened and drained. Inflammatory exudates are separated and entered with the finger whether they be in the cellular tissue or in the pelvic cavity. The technic of this procedure will be described later.

When there is pus in the pelvis the vaginal should be the route of election, because it gives better drainage, it is safer, gives less shock, and is followed by less danger of intestinal adhesions. Recovery is less complicated and more rapid than by abdonimal section.

If it is desired to enucleate the diseased ovary or tube, the abdomen may then be opened at the same sitting with less danger and greater facility, or should it be necessary to perform a subsequent operation, the difficulties would in no way be increased.

In operating for chronic gonorrheal tubal or ovarian infection, it is my custom to curette the uterus and at that time to examine carefully the pelvic fornices for any induration or exudate which would indicate an involvement of cellular tissue. Should any induration be found, it should be incised and explored with finger and then drained with gauze. The abdomen is next opened and should the structural changes have gone so far in the tube as to render it useless or a menace to health, it is extirpated in its entirety or a plastic operation done for its conservation.

The treatment of pelvic injection, caused by the streptococcus, is the same in regard to the palliative means as that of the gonococcus. Some cases recover with rest in bed, cold applications to lower abdomen, restricted diet, hot vaginal douches, saline cathartics, and opiates, if needed. As the uteri of many of these cases have retained products of conception, sloughing masses, or infected blood-clots, they should be cleaned out with great care either with the finger or the blunt curette, great gentleness being used to avoid opening new avenues of infection. This should be followed by an intrauterine douche of sterilized water or a mild antiseptic. If the infection follows an operation upon the cervix or perineum, the stitches should be re-

moved and free drainage established. However the infection has occurred, the treatment is now the same. Knowing that the infection of the streptococcus travels by the lymphatics and along the blood-vessels in the cellular tissue and rarely along the mucous membrane, the periuterine tissue and the fornices should be carefully palpated, and if any induration is found, it indicates that the process has extended beyond the uterus, and vaginal incision and drainage should immediately be performed.

When the diagnosis of pus in the pelvis is made, no time should be lost in evacuating it, whether the condition be acute or chronic, provided it is done by the vaginal route. Dense hardness in the cellular tissue means pus. The induration should be explored thoroughly with the finger, and the pelvic contents examined bimanually at the same time. If the pus is found to be intraperitoneal, in the tube or ovary, the culdesac is opened and the abscess evacuated and drained.

As mentioned before, it is my custom, in chronic cases of infection of the tubes and ovaries, when it is desirable to do conservative work or to extirpate the appendages, to open the abdomen, but not before having curetted the uterus and opened into the cellular tissue, should any induration be found.

In the early years of the study of diseases of women the infection of the cellular tissue was considered the prime factor in all pelvic inflammations, and all local measures were directed to the relief of this condition. That many cases resisted this treatment and remained unrelieved is not surprising in the light of our present knowledge. With the advance of abdominal surgery it was observed with such frequency that pelvic inflammation was caused by infected tubes and ovaries, that many laparotomists deny the primary infection from any other source and totally ignore the existence of plevic cellulitis.

For some years I have felt convinced that the pendulum has swung too far toward the tubes and ovaries and too far away from the cellular tissue with its dense network of lymphatics and blood-vessels in the treatment of pelvic infection.

Since inflammation of all these tissues occur conjointly or separately, the rational method would be to direct the treatment to the tissue affected, whether it be of ovary or tube or cellular tissue, or of all combined, as frequently happens.

In recent literature little has been written about pelvic cellulitis. The German authors have recognized the condition more than have the English or American. In American text-books it is mentioned casually by some and is ignored entirely by others. The best article upon pelvic cellulitis that has come to my notice is by E. C. Dudley, in his "Principles and Practice of Gynecology," and from which I quote: "Clinical experience shows pelvic suppuration to be primarily almost always in the tube; rarely in the cellular tissue below; and if perchance an abscess be found there it usually gives evidence of having burst from the tube into the broad ligament. The above facts have led to a tendency of late years especially, among the laparotomists to deny the existence of pelvic cellulitis and to announce the triple proposition; that cases of extrauterine pelvic inflammation are, except in rare instances of puerperal origin, essentially of tubal development; that ovaritis and peritonitis are always secondary to tubal disease; and that an abscess in the broad ligament is there only when a previous infection of the Fallopian tube has forced its way through the mesosalpinx into the parametrium. In this connection, let us remember that the disease occurs in men who have no Fallopian tubes. Why should the cellular tissue of the pelvis be free when the same tissue in every other part of the body is subject to infection? Would it not be just as reasonable to assume that pleuritis is the central lesion in all pulmonary infection or that perinephritis is the essential factor in all cases of contracted kidney? The question, however, is not settled by a *priori* reasoning. Postmortem studies prove the frequent existence of acute cellulitic abscess, not only by rupture of a sactosalpinx into the parametric cellular tissue, but also by the direct lymphatic or venous route."

It is not my object to prove the existence of pelvic cellulitis as a primary infection, but rather to call attention to its existence whether it be primary or secondary or whether it be called "perilymphangitis" or "periphlebitis" and to suggest its treatment along the same lines as is employed in the cellular infections in other parts of the body. Since the infecting bacteria are the same and the tissue is the same, this seems but rational. The treatment of infected cellulitis is incision and drainage, and this should be performed whether the infection be primary or secondary to intrapelvic inflammation. In the latter case this should be done in conjunction with the intrapelvic operation, whether it be abdominal or vaginal.

Those operators who remove the uterus when both appendages are affected with suppurative disease, do so for drainage, not of the pelvic cavity, because that could be done easier through the culdesac, but for drainage of the lymph spaces and cellular tissue. This drainage could be accomplished before entering the pelvic cavity by

dilating and curetting the uterus and by opening and draining the cellular tissue wherever induration is felt, and thus the removal of the uterus be avoided.

I have recorded fifty-three vaginal sections for suppurative disease of the pelvis without a death and without an accident, and in but one instance was a subsequent abdominal operation performed. The patient had a large pyosalpinx on one side, which was opened and drained from the vagina. She recovered promptly and remained well for three months. The other tube and ovary which had appeared healthy at the time of operation became the seat of active suppuration and demanded operatiove interference. As this patient had a fibroid of the uterus and was forty-nine years old, it was thought best to perform abdominal hysterectomy and remove the suppurating appendage at the same time. This was accordingly done, and the patient made an uneventful recovery.

The technic that I have followed in performing posterior vaginal section differs somewhat from that recommended in text-books or from any that has come to my notice. It is briefly as follows: The patient is put in the lithotomy position and prepared as usual. The posterior vaginal wall is depressed by a perineal retractor and the posterior lip of the cervix is seized with bullet forceps and elevated until the culdesac is obliterated and the tissues put on the stretch. The mucous membrane of the posterior wall of the vagina is then seized with another pair of bullet forceps at a point about an inch and a half below the cervix and in the middle line. Slight traction upon the lower pair of forceps will raise a vertical fold of mucous membrane behind the cervix. This fold is cut transversely with a pair of sharp-pointed scissors at a point just below the junction of the vagina and cervix. The cut is then enlarged on each side and with the finger the mucous membrane is separated from the peritoneum. If it is desired to enter the peritoneal cavity, the peritoneum is put on the stretch by means of the fixation forceps and snipped with scissors. The finger is then introduced and acts as a protector and guide, while the opening is enlarged by lateral cuts with scissors until the desired width is reached.

By this method the necessity of introducing the finger into the rectum is avoided and all tissue is felt before being divided. I have never found it necessary to make a vertical incision in addition to the transverse, in order to gain the required space. Two fingers are now passed into the pelvis and a careful examination made. Collections of pus can usually be entered with the fingers, and it is my custom to penetrate in this way all indurations whether they contain pus or inflammatory exudates and wherever they are situated and whether they fluctuate or not.

If the pus is contained in the tube and the tissues are too dense to penetrate with the finger, a long retractor or possibly two are introduced into the culdesac and the pyosalpinx brought into view and opened. All pus collections having been opened, the question of irrigation comes up. From my experience I prefer not to irrigate immediately, but after the first dressing, which is usually on the fourth day, because there seems to be less reaction and less to drain if irrigation is not practised at the time of operation. The most important feature of this operation is the drainage, and upon this depends the success of the procedure.

Formerly rubber-tube drainage was invariably used in the culdesac, but now gauze is usually employed, because experience has shown that with the latter there is less temperature, less pain, and less care is required than when the tubes are used. The rubber tube increases the suppurative process. The directions usually given in text-books and the method practised by most surgeons is to pack the cavity lightly with a strip of gauze and drain into the vagina. This often results in a rise of temperature in a few days and the premature closing of the vaginal incision, because the strip of gauze passed into the vagina, cannot efficiently drain the mass above and the vaginal incision closes down upon the strip and locks up the secretions.

The method that I have used for the last ten years, and with most satisfactory results, was suggested by Dr. E. P. Mallet. In this, rolls of gauze, made after the manner of the "cigarette drain," are used. These rolls are about one-half to three-fourths of an inch in diameter, and are long enough to reach pus cavities in any part of the pelvis. They are introduced with forceps either by sight or are guided by a finger of the other hand and passed through the vaginal incision into each pus cavity of diverticulum. The number of drains used depends upon the size and number of the pus cavities; from two to six are generally required. This arrangement of drains prevents the incision from closing and checks the hemorrhage of small vessels by pressure, and yet does not interfere with the drainage, for the secretions pass through the gauze and through the spaces between the rolls. It is my custom to use the rubber tissue covering for the rolls, to facilitate their removal, but this is not essential. The drains remain in place until the fourth day, unless there is considerable rise of temperature, and in that case they are removed earlier. When they are

removed, the cavity is irrigated with peroxide of hydrogen and followed by a saline solution, and a smaller number of rolls of gauze are introduced. This dressing is repeated every second day and the number of drains diminished until the drainage ceases and the incision is allowed to close. After the operation the patient is placed in the so-called Fowler position until after the fourth day, when she is allowed to sit up.

Among the patients operated upon, collections of pus were found in one or both tubes, in the ovaries, in the tubes and ovaries combined (tuboovarian abscess). Pus was found in the culdesac, in the cellular tissue anterior to the uterus and in the folds of the broad ligaments.

As most of these cases were hospital patients, it has been impossible to follow many of them in after-life. Within the past year sixteen were traced, and they all reported to be in good health.

One of these was a case of ovarian abscess which was incised and drained thirteen years ago, and she has remained well ever since. This case was remarkable because the tubes and other ovary appeared to be perfectly healthy, and yet the infection was undoubtedly gonorrheal, showing that the infection of the ovary probably occurred through the lymphatics.

Another patient was a chorus girl who had two large tubal abscesses undoubtedly gonorrheal. They were incised and drained seven years ago, and she has followed her vocation with comfort ever since

In several of these cases of pus in the pelvis it was necessary to explore the pus cavity and break up the adhesions two and, in one case, three times before a cure resulted. This was done with the finger while the patient was under chloroform. These subsequent procedures were made necessary by overlooked abscesses in the pelvis or too early removal of the drains.

No subsequent pregnancy has occurred among this class of my patients.

In 1895 it was my pleasure to hear the late Dr. F. Henrotin read a paper before the American Gynecological Society, entitled "Conservative Surgical Treatment of Para- and Periuterine Septic Disease." It was a strong plea for early vaginal incision and drainage in acute cases of pelvic inflammation, and impressed me so much that I have practised that method whenever the opportunity offered. As Dr. Henrotin has said, these acute cases are seldom seen in the hospital operating-rooms, but frequently in consultation. The two cases related by him were infected by the streptococci, but as the histories of the others were not given, the nature of the bacteria is not mentioned, but the principle of early operative interference was carried out.

A certain proportion of cases of infection, whether gonorrheal or streptococcic, get well without involving the appendages or the lymphatics, and therefore the accepted teaching is to do nothing beyond palliative measures or possibly to curette until collections of pus form or systemic infection occurs; then they are operated upon with considerable risk to their lives and their pelvic organs.

The rule should be that whenever infection has extended beyond the uterus, as shown by induration of the cellular tissue or swelling of the tubes, vaginal incision and drainage should be performed. I have followed this method in eleven cases presumably of streptococcic infection, and the results have been most satisfactory.

One was a postoperative case. The patient was a young married woman. She had been curetted, her cervix and perineum repaired. The abdomen was then opened and her appendix removed and uterus suspended, all at one sitting. The ovaries and tubes were found to be normal. There was little or no reaction, and her recovery seemed all that could be desired. On the fourteenth day, having a normal temperature, she was permitted to sit up in bed, and was to have been out of bed on the day following. She was taken with a severe chill and her temperature and pulse were found to be 103° and 110, respectively. She had no localized pain or tenderness, but felt and looked extremely ill. Twelve hours later her temperature had reached 104° and pulse 120. She was examined carefully and nothing was found to account for her condition. The cervix and perineum had healed, and the catgut sutures had disappeared. In another twenty-four hours, or two days after the beginning of the attack, her temperature in the night registered 105.8° and pulse 130. The next day or the third of her illness some induration was felt behind and to the left of the cervix. This induration was so slight that it seemed hardly possible to account for her symptoms, but no other abnormality could be found. She was immediately put under an anesthetic and the mucous membrane behind the cervix was divided with the scissors as before described. The finger was inserted into the cellular tissue and the indurated mass penetrated and drained with two cigarettes. The induration was at the base of the left broad ligament, and no pus could be dis-

tinguished when it was opened; only what appeared to be serum and some pyogenic tissue. As all else in the pelvis appeared normal, there was nothing to do but await results. Her leukocyte count the day the vaginal incision was made was found to be 30,000. In a few hours after the vaginal incision her pulse and temperature began to go down, and she improved almost as rapidly as she had become ill. On the fourth day after this operation she had another rise of temperature, this time to 103°, and it was found that the drains had been removed too soon and the secretions retained. The opening and the cavity were then enlarged with the finger and more drains introduced, and the temperature went down promptly and the recovery was uninterrupted.

Another case was that of a young married woman seen in consultation. She had missed two periods and had had an abortion induced. When seen on the third day of her illness her temperature was 102° and pulse 120. The uterus was large and boggy, but quite movable; no induration was felt in the cellular tissue. The uterus was then gently curetted and some products of conception removed. After this she improved for two days, and her temperature and pulse went down to nearly normal, but on the third day after the curetting she began to complain of intense pain in the pelvis and her temperature went up to 103°. At this time an examination revealed an indurated mass in the upper posterior wall of the vagina between the culdesac and the rectum.

The patient was immediately anesthetized and a transverse incision made behind the cervix. The finger was introduced and the mass penetrated. Bloody serum was liberated and the cavity drained with two rolls of gauze. In a few hours the pain subsided and the temperature began to go down, and by the fourth day, when the drains were changed, the temperature and pulse were normal. The patient made an uninterrupted recovery.

Another case, very similar to the last, was that of a young woman who had gone ten days over her period. She had attempted to bring this on by means of a rubber catheter containing a stylet. By standing with one foot upon the seat of a chair and the other foot upon the floor, she had passed this instrument into the uterus. The operation was followed by some bleeding and pain, but to make assurance doubly sure, the instrument was introduced again on the following day and more bleeding resulted. The next day she had a chill and high fever and intense pelvic pain and a moderate flow. She was seen by me on the seventh day. Her temperature was 104° and pulse 130. The uterus was larger than normal and fixed in the pelvis and excessively tender. An indurated, ill-defined mass was felt on the left side of the cervix. An immediate operation was advised and performed the same day. The uterus was curetted, and a posterior vaginal incision was made and the finger was worked into the tissue and the mass penetrated. It proved to be an abscess in the left broad ligament. About an ounce of pus was evacuated, and the customary drains were inserted. The recovery was rapid and uneventful.

In the three cases mentioned the peritoneal cavity was not opened, but it would have made no difference had it been, for in several other cases the peritoneum was penetrated and no harm resulted.

The treatment of acute gonorrheal salpingitis and ovaritis by vaginal incision and drainage is simplified in many cases by the fact that when suppuration occurs in the appendages, the swelling is so great that they gravitate into the culdesac, where they can be easily reached from the vagina. If the tubes are not palpable the inflammation is probably not virulent and recovery will occur spontaneously, but if the tubes can be palpated or there is induration in the cellular tissue, then vaginal incision and drainage should be performed. Care must be exercised in the after-treatment of these cases because of the tendency of the opening in the tube to close and stop the drainage, but by attention to this detail, many tubes can be saved from further disorganization and restored to usefulness.

Before performing vaginal section the uterus should always be curetted thoroughly and an application of pure carbolic acid followed by alcohol be made to the endometrium.

In this communication the writer has endeavored to call attention to the importance of early vaginal section and drainage in pelvic infections, its value in all cases of pelvic suppurative disease, whether acute or chronic, and to urge the drainage of inflamed cellular tissue by vagina, especially in those cases where the appendages are removed by laparotomy and the uterus was formerly sacrificed in the so-called radical operation. By the use of this drainage it will not be necessary to remove the uterus for the relief of symptoms. The uterus in itself is a relatively harmless organ, and the symptoms attributed to it are caused by periuterine inflammations and adhesions—much more frequently by the periuterine inflammation than by adhesions.

The patients suffering from pelvic infection are usually young women, and the loss of their ovaries and tubes is of considerable importance to them as the symptoms of artificial menopause are usually pronounced and the atrophic changes frequent; but the ultimate results in this class of cases is fortunate as compared with some that come under observation after the uterus has also been removed. In them senile atrophy occurs to such an extent that sexual intercourse is prevented or interfered with or they are rendered miserable by a senile vaginitis that resists all forms of treatment. They become mentally morbid and are unhappy in their domestic life. One of these patients will do more to prejudice the laity against surgery than all that could be written or said by mental healers or osteopaths.

At the present time these unfortunates are not so numerous as in former years. If by early surgical intervention disease may be arrested and tissue and organs saved, then an important step in true conservatism has been made.

SUPRAPUBIC OPERATION UPON THE PELVIC FLOOR FOR PROLAPSE OF THE UTERUS.*

(With eight plates.)

W. M. Polk, M.D., LL.D.

On January 5, 1909, P. D., a widow, 43 years of age, doing housework for a living, was admitted to my service (Ward 23), at Bellevue Hospital. The following is her history from the records:

Diagnosis—Prolapsed uterus and cystitis.

Operation—January 8, 1909.

Family History—Father killed in battle; mother died of old age; one sister and two brothers dead, cause unknown, one brother living and well. No tubercle bacilli, kidney or brain diseases or any similar condition to that which patient complains of.

Married eleven years. Miscarriages, six.

Widowed four years. Menopause, 1906.

Previous History—Remembers no diseases of childhood. Has always kept well as an adult except for present condition. Injuries, none. Operations, none.

Menstruation—Began at eleven years and was regular every twenty-eight days, lasting four days, with little pain and discomfort, until time of first miscarriage, 1894; since that time menstruation has been regular (except when pregnant), and painless, but has lasted from ten to fourteen days with much bleeding. Menopause in July, 1906, was easy.

Pregnancies—In the summer of 1894 patient had her first miscarriage at six months, due to a fall. In bed fourteen days and felt well afterward except for sensation of weight in region of uterus. 1895, second pregnancy, a miscarriage at six months, was spontaneous without known cause and patient remembers no particulars except that it was easy. 1897, third pregnancy with delivery of a dead seven months' fetus spontaneously; patient was in bed for eight weeks and was very sick following event. 1899-1901, fourth pregnancy occurred sometime during this period; spontaneous delivery at six months; no after effects. 1901-1903, fifth pregnancy like fourth. 1904, sixth pregnancy in March, like fourth and fifth.

Vesical symptoms, not annoying.

Vaginal discharge, none.

Venereal history, none.

Habits, coffee and tea in quantities; no alcohol.

Bowels, regular.

Present History—One year before admission patient says she fell downstairs while carrying a hod of coal and the next day noticed a mass like a ball protruding slightly from the vagina. The mass was not particularly sore or tender but would not remain when replaced in vagina, and has continued to get larger and larger up to present time. Patient has lost thirty-one pounds in the last four years, since husband's death but attributes it somewhat to hard and unusual work as she was forced to support herself. Has had a good appetite all the time and states positively that she has had no discharge or pain. She is very thin, looks ten years older than reported,

* Read before the American Gynecological Society, April 20-22, 1909.
Reprinted from the American Journal of Obstetrics, Vol. LX, No. 3, 1909.

and has evidently suffered much hardship, but full of courage and determination to care for herself, in fact insists on immediate operation that she may return to her work.

Examination shows complete eversion of the vagina and with it prolapse of the entire uterus. Slight traction upon the cervix enables one to coaptate the vagina,

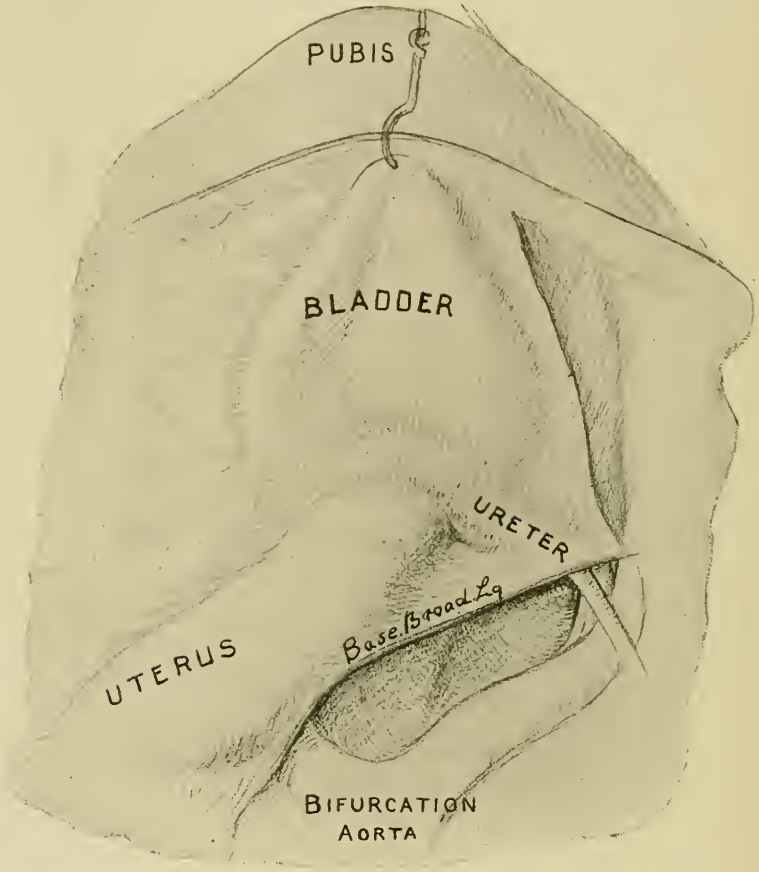

Fig. A.—Anatomical.

above the fundus, and outline the entire organ below this. The bladder is drawn down with the mass, as proved by the sound. The rectum has separated itself from the everted vagina and is in fairly good position.

Five days from admission I operated. Upon opening the abdomen, instead of the usual condition of the pelvic floor, slightly concave, with the uterus and broad ligaments standing out prominently above it, I found a pit with the uterus sunk well down therein, the base and posterior face of the bladder dragged down with it, the broad and round ligaments reaching up above it to the pelvic brim like arms thrown up above the head; in similar, but in less pronounced manner, the uterosacral ligaments ran up to their attachment on the sacrum. Seizing the fundus, the uterus and its attachments were drawn easily upward, till it stood above the pelvic brim, the ligaments reaching downward behind, to the face of the sacrum, at the sides to the pelvic brim. There was complete relaxation, with elongation of all the interpelvic supports of the uterus, vagina, and bladder. I operated so as to shorten them. The uterus was removed, as the woman had passed the menopause. The separation of the bladder, suturing of the vagina, of the peritoneum and underlying fibro-connective tissue, the broad and uterosacral ligaments, was done as described in the paper I append. The only departure made was in dissecting out the ureters before passing the sutures;

namely, those deep which dealt with the vagina, those higher which dealt with the fibro-connective tissue and peritoneum. The dissection satisfied me, that the work could be done equally well without this step.

I now beg to submit the operation to your criticism, not only as presented in this paper, but in the person of the patient who comes here to submit herself to your examination.

Suprapubic Operation Upon the Pelvic Floor for Prolapse of the Uterus.

The operation is designed to aid in the correction of all degrees of prolapsus uteri, but *particularly its ultra forms.*

Having an extreme case, one with the uterus, the base of the bladder, and a good part of the vagina outside the vulval opening, the patient is placed in bed and there treated for a week or ten days. This is for the purpose of reducing the prolapse, and permitting the affected viscera and surrounding structures to regain as much of the normal status as possible. As good a condition local and general as can be gotten in the case being secured, the operation is performed.

After opening the abdomen, the Trendelenburg position secured, and the pelvis (the true pelvis) cleared of all intestine but the lower sigmoid and rectum, the uterus

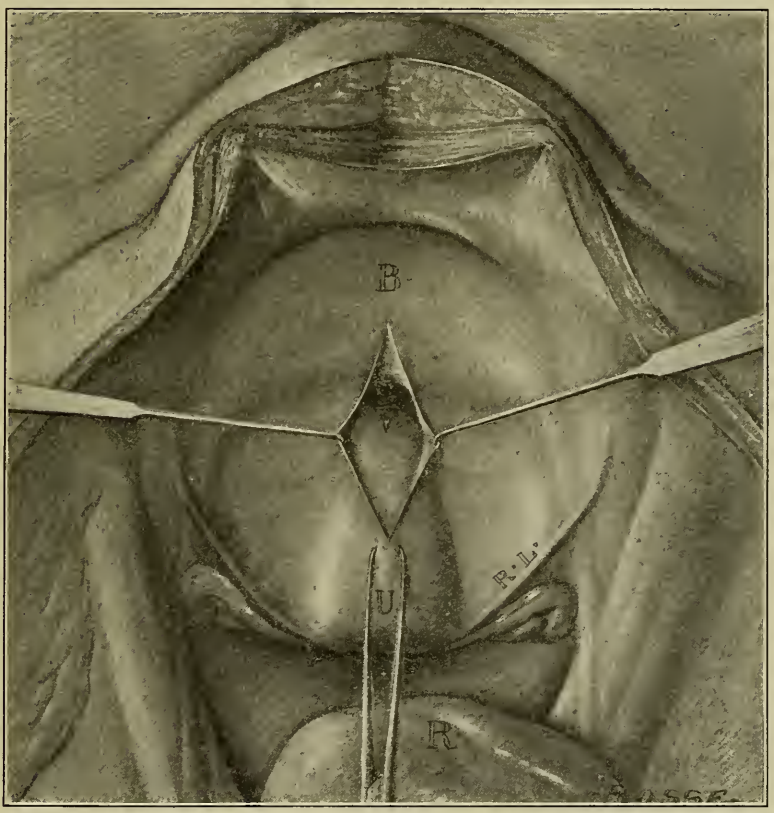

Fig. 1.—Utero-vesical space opened. Uterus retained or removed, as operator determines.

is firmly caught with a double tenaculum at its anterior vaginal juncture. Pulling it up and making the vagina taut, an anteroposterior incision is made reaching from the tenaculum to the bladder (which meanwhile is held against the pubis), and extending through tissue to the recognizable vaginal wall (Plate I). Through this opening which is stretched laterally, the bladder is separated from the face of the vagina as far as the trigone or even somewhat beneath it. The ureters are pushed aside, and where

they turn in toward the trigone, are displaced upward and forward with the bladder. In this maneuver the anterior face of the vagina is adequately exposed beneath the bladder, but this must also be done as far up as the site of the tenaculum. As you know, this is an easy task. The next step is to unite by suture with continuous kangaroo tendon the anterolateral lines of the vagina (one on each side), from below

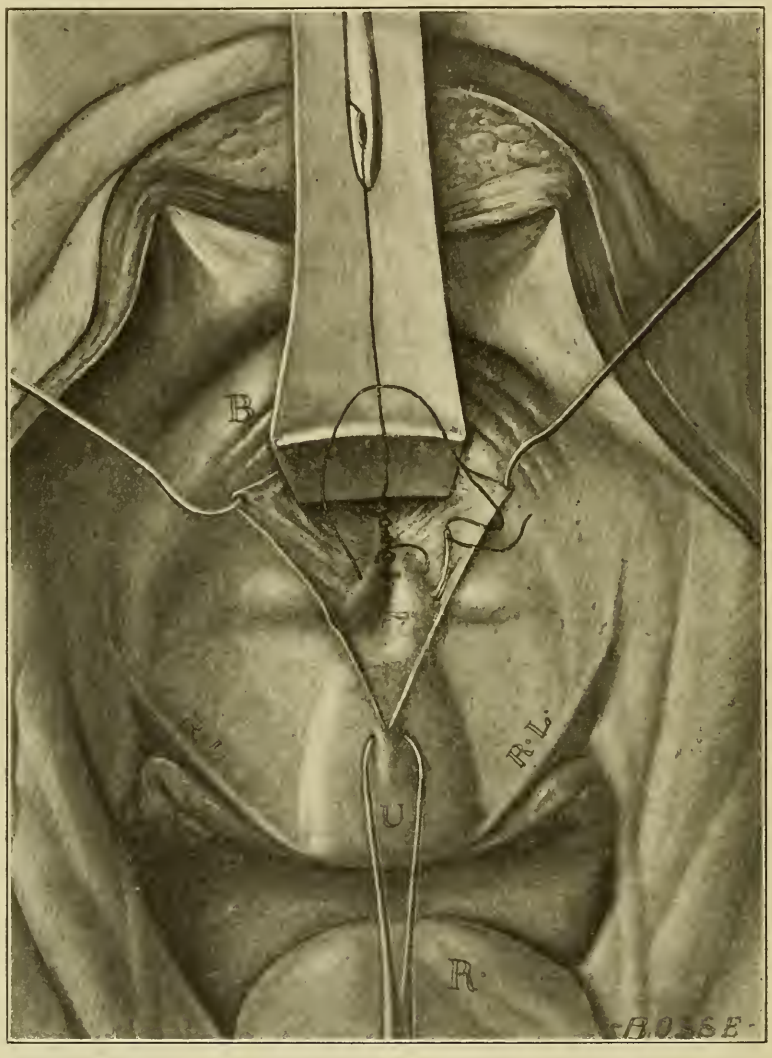

Fig. 2.—Plication of anterior wall of vagina.

upward, beginning as far down as possible and ending just below the upper end of the original incision (Plate II). To secure proper exposure, the bladder, after separation, is held forward with a broad retractor The suturing is done with a short, stout, curved needle, aided by a hook with which the vagina at the point of suturing is caught up and directed toward the point of the needle. Another method is to use the fingers of the disengaged hand—in the vagina to lift it up—stitching down upon them. It is not necessary to penetrate into the vaginal cavity, but if done no harm will accrue, the surface having been already carefully prepared. A second line of continuous kangaroo suture is now placed, so as to draw to the median line as much

fascia and covering peritoneum as can be brought in from the sides of the bladder, the vagina and the uterus (Plate III). The structures in this region which must be left outside the sutures, are the ureters and the uterine arteries—the arteries are in danger at the upper end of this field, the ureters at the lower. Both can be outlined by careful fingering of the tissue as the sutures are passed; this is easily true of the vessels, and I believe also of the ureters, but in view of the greater harm coming from their injury, they can be outlined by prior catheterization, or if not, readily exposed by blunt dissection, where they curve inward to the upper outer angles of the trigone. This second line of sutures, as intimated, must be entered far enough from the edge

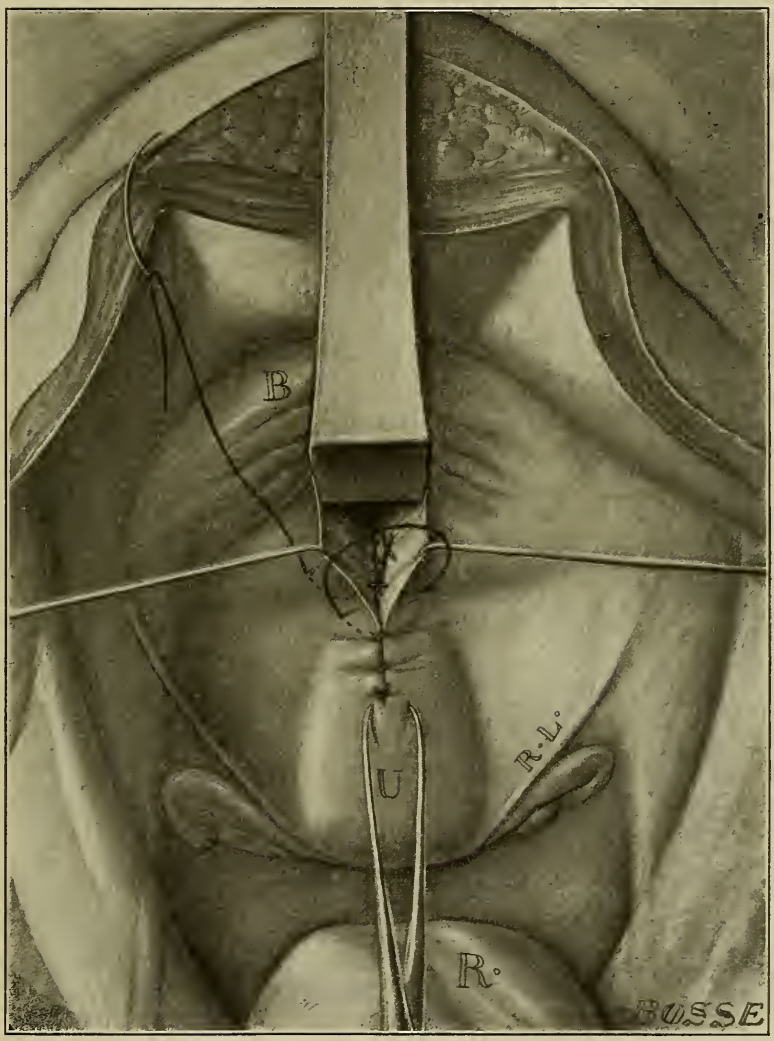

Fig. 3.—Uterus retained or removed, as operator determines.

of the incision to take up all slack tissue and in passing, follow an oblique direction from the point of entrance upon peritoneal surface, downward and inward toward the sutured line of the vagina, into which it may pass, then into the fascia at opposite vaginal edge and so on obliquely upward and outward so as to include here also all slack tissue. The most important loops of this suture are those employed at the lower

portions of the incision—the last two, need not enter the vaginal tissue, but, going down to it, pass over, and then out on the opposite side as before. Their effect will be to accentuate the line of the bladder base, in fact carry it in further beneath the bladder and fold in some of its tissue (Plate IV). As will be seen later in bringing out the anatomical feature of the subject, the suspensory ligament of the bladder is shortened

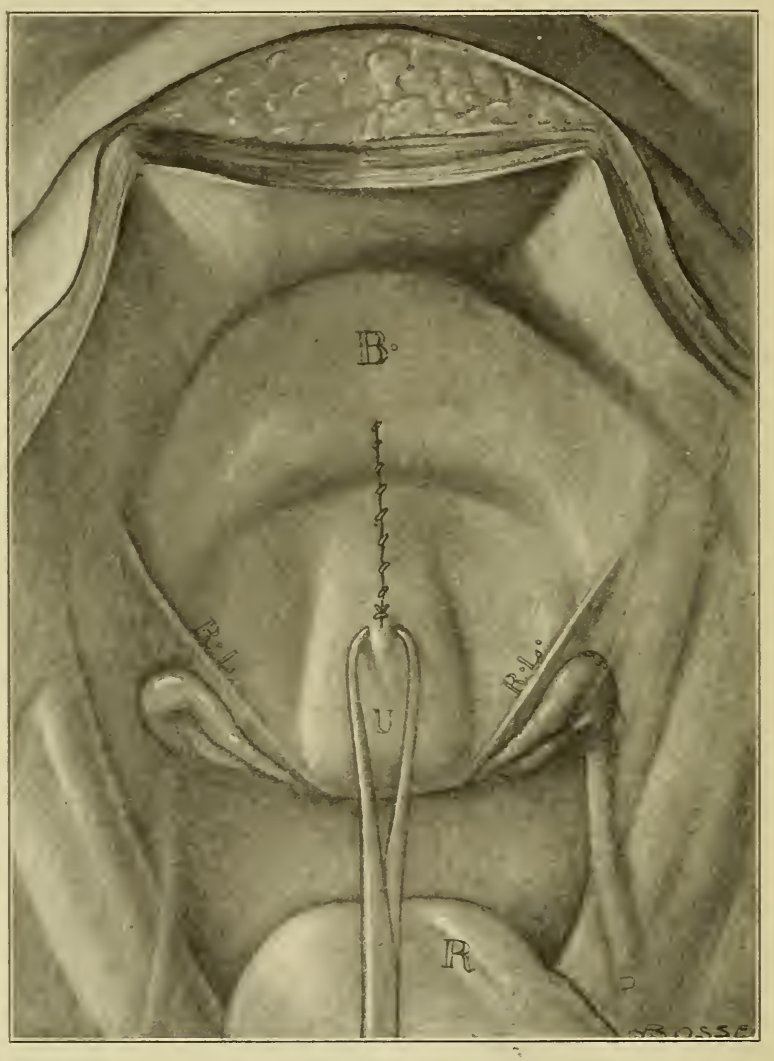

Fig. 4.—Anterior plication finished.

in this maneuver, as well as the lateral fascial connections of the vagina (which merge with the lateral supports of the bladder below, and the broad ligaments above, serving the purpose of ligaments), and the basic lines of the broad ligaments. It now remains to shorten the uterosacral ligaments. These are caught up at about the junction of the inner and middle thirds, drawn in from this point and stitched with the same suture material either to the inside, below, or to the outside of their uterine attachment, as is most easily done. It is essential to take in as much of the slack as is needed to give them their original supporting function (Plate V).

The question as to the disposition of the uterus should be settled at the outset of the operation. If to be retained, the operation as described will be carried out with the addition, if deemed best, of shortening the round ligaments, but this is not essential. If it is a senile uterus, I suggest it be thrown forward and the fundus held in the sulcus behind the bladder by a retaining suture through the round ligament at each cornua (Plate V). This for the purpose of utilizing in this region all the aid the round ligament and remaining parts of the broad ligament can furnish as supports. If the uterus is removed, the variations from the operation as described relate to the treatment of the broad and uterosacral ligaments. The operation is then to be executed as described as far as the completion of the suturing in front of the uterus, then this organ is dissected or cut from its lateral attachments to about the level of the internal os, care being taken to stop short of the attachment of the uterosacral ligaments. The cut surfaces of the stump are now stitched together in continuation of the line of

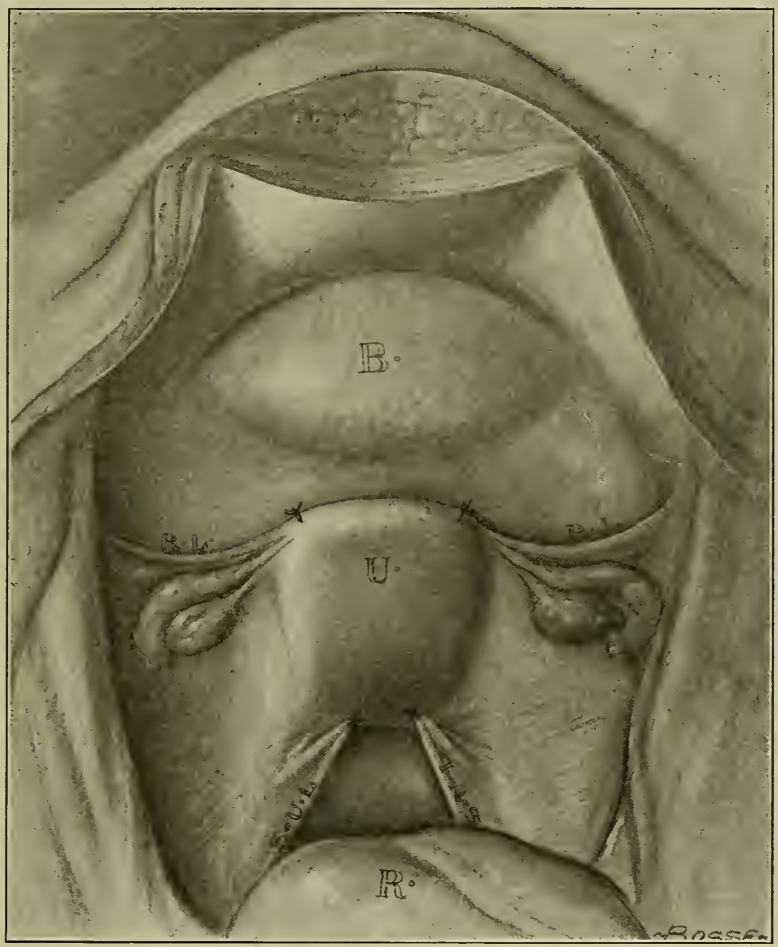

Fig. 5.—Senile uterus retained and held forward.

original incision; the loose ends of the severed broad and round ligaments caught up and included in this line of suturing (Plates VI and VII). And finally the uterosacral ligaments are caught up at the junction with the stump (Plate VII); the right is drawn over and stitched to the stump to the left, and the left is drawn to overlap the right and stitched in corresponding position to that given the left ligament (Plate

VIII). The elongation and relaxation of all these tissues make the several steps of the operation easier than one might infer from an experience confined to the normal pelvic floor.

With the completion of any one of the procedures outlined, the superapubic operation upon the pelvic floor will have been finished. After closing the abdominal wound,

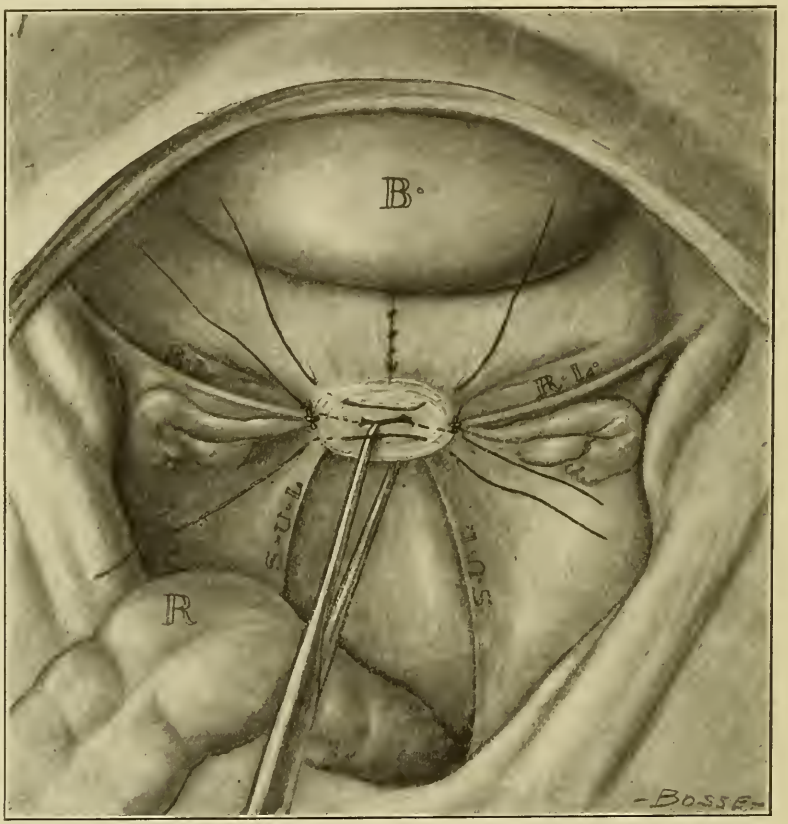

Fig. 6.—Uterus removed. Round and broad ligaments attached to stump.

further procedure can be determined by the patient's condition. It remains only to operate upon the perineal structures. If much is needed, then no doubt it will be best to postpone operation, otherwise, do it at once, applying any one of the operations upon the levator ani, lower posterior vaginal wall (rectocele) and perineum, the operator prefers.

Dr. Polk presented the patient for examination at the conclusion of his paper.* Professor Pozzi, for the committee, submitted the following report:

New York, 27th of April, 1909.

I examined the case of procidentia uteri operated on by Dr. W. M. Polk by *Suprapubic Operation Upon the Pelvic Floor*. The patient was of a delicate complexion, about fifty or sixty years old. She had suffered for years and had been operated on about four months ago. I found that the vagina had a normal depth. Around the neck of the uterus was a plastic infiltration, but no pain by pressure. I think the result is excellent.

(Signed) Prof. S. Pozzi,
Honorary Fellow of the
American Gynecological Society (Paris).

* July 12, 1909. I examined the patient to-day, she being in the standing position. The plastic infiltration around the neck of the uterus has disappeared; in other respects the conditions are identical with those named in Professor Pozzi's report.—W. M. P.

Anatomical Suggestion.

In estimating the need for this operation it is best to view the anatomical conditions from the standpoint of the living subject rather than that of the cadaver, the principal reason for this being the fact that in the cadaver, owing to position as well as to the contraction of tissue which takes place, the space between the peritoneal and muscular (levator ani) layers (or surfaces) of the pelvic floor is materially lessened, the peritoneal face approaching the level of the muscle to a far greater extent than is witnessed in the normal living pelvis. This statement is borne out by the dissections which we have from time to time made upon the suprapubic aspect of the pelvic floor in connection with the requirements of hysterectomy and other forms of suprapubic operations upon the pelvic viscera. The peritoneal surface and the muscular surface (levator ani) of the pelvic floor may be said, speaking broadly, to start from the inner face of the pubic bone at about the same level. As we follow the general line of the two surfaces backward, however, they diverge and we find there is a gradually increasing depth in the space between them which is filled with fibro-connective tissue, which in turn presents throughout its meshes sundry lines of condensation of sufficient density and strength to serve as supports or ligaments to such structures as they accompany or to which they are attached. Muscular fibre

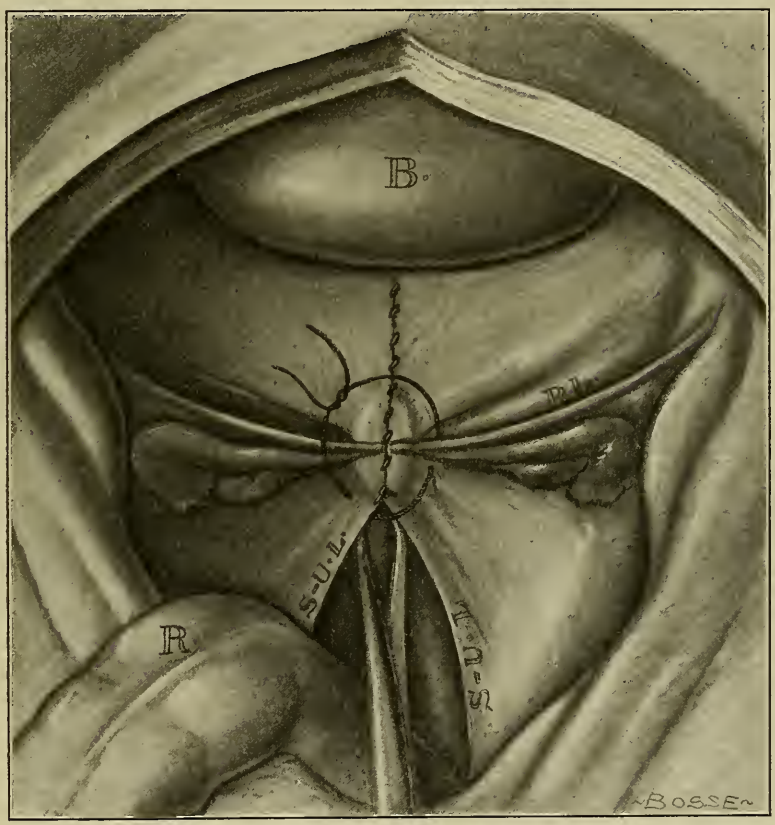

Fig. 7.—Uterus removed. Stumps of round and broad ligaments coaptated.

analogous to that belonging to the outer coat of the uterus and vagina exists in some of them, notably the uterosacral and broad ligaments. The breaks in the peritoneal face of the floor are Douglas' culdesac behind, vaginal opening in the centre, and the vesical region in front. The break at the vesical region conforms to the base of the bladder but it finds compensation in the close proximity of the puborectal division of the levator muscle, as it envelopes the vagina in its course backward to the perineum.

That at the vagina is protected by support from the broad and uterosacral ligaments; the upper part of the broad and round ligaments belongs to the body of the uterus projecting above the plane of this floor, and gives but indirect aid at this opening. The break in the floor at the culdesac is for the accommodation of the rectum, but the uterosacral ligaments guard it. They represent the posterior confines of the peritoneal level of the pelvic floor, and their strength is sufficient to resist any direct pressure they may be subject to. They yield however to forward and downward traction such as comes from prolapse of the anterior pelvic floor, becoming thereby party to vaginal, and especially uterine prolapse. Just here it is pertinent to say that the break in this contour of the upper floor is compensated by the natural descent of the anterior rectal wall, which thus fills it with part of a self-supported viscus; and also by the relatively smaller degree of intrapelvic pressure to which it is exposed The

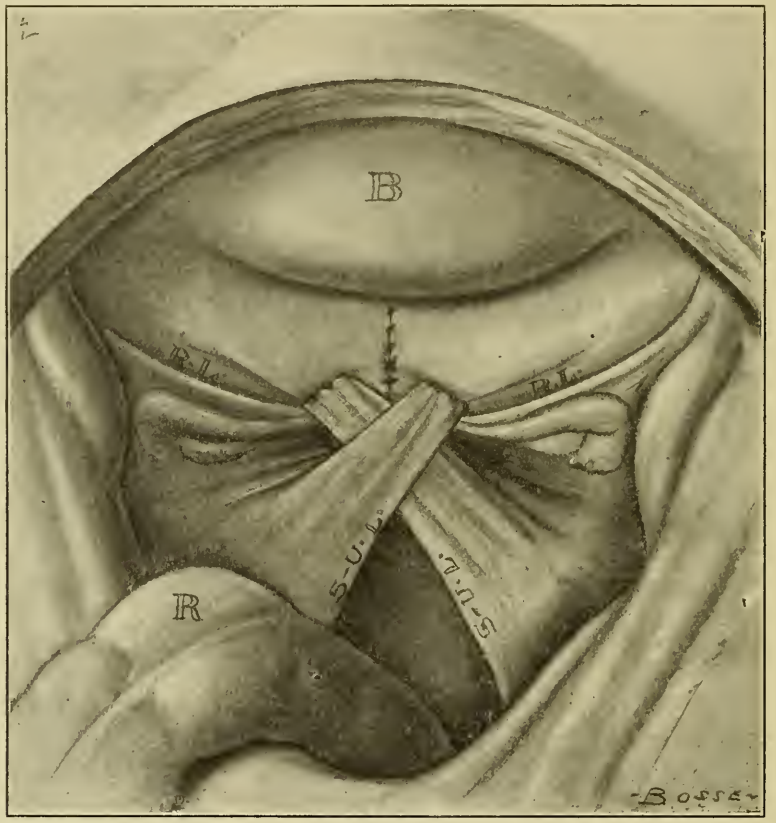

Fig. 8.—Uterus removed. Utero-sacral ligaments thrown forward and crossed over stump.

distance between the two principal floor layers, peritoneal and muscular, is here at its greatest. Measured by the sacral curve, it extends from the second sacral bone to the coccyx—the direct distance is shorter in proportion to the curvature of the sacrum. The breaks in the muscular layer of the pelvic floor are the urethral, vaginal and anal openings. The first may be ignored, of the remainder, the vaginal is of prime importance, but as our operation does not directly involve the muscular floor we stop at this mention of its openings. Both floor layers are swung from the pelvic wall, the peritoneal-fibro-connective, at a higher level than the muscular; both are convex downward, the muscular much more so than the peritoneal in consequence of which they are much farther apart at the median line than at the walls of the pelvis. The vagina extends directly through this median region, and closely associated with its lower anterior half we have the base of the bladder, the portion of that organ which,

as we have said, occupied the break in the forward part of the peritoneal-fibro-connective layer of the pelvic floor.

Turning now to the condensations of this inter-lying fibro-connective tissue, we find they have an important bearing on the vagina and bladder.

The principal lines or areas of condensation are about the sides and posterior aspect of the uterovaginal junction (the vaginal break in the upper floor layer) and are known anatomically as the lower lines of the broad and the uterosacral ligaments; here you find the involuntary muscular fibres derived from the vagina and uterus, interwoven in such fashion as to add strength to the structures. As we descend, the condensation continues, being in part a continuation downward upon the vagina of both the uterosacral and broad ligaments, but it is to be noted that the actual support is much more direct to the lateral and posterior aspects of this viscus than to the anterior. This arrangement continues well below the bottom of the culdesac. The normal tonicity of the vagina, especially in non-parous women, compensates the anterior wall for this lack of direct support from this direction, but after the stretchings of child birth, particularly in the face of faulty involution, this part of the vagina must proportionally rely for support upon other and more direct lateral and anterior agencies to be now mentioned, viz.: An important line of this condensed tissue accompanies the ureters. It takes form as they pass through the base line of the broad ligaments at junction of outer and middle thirds, increases in thickness as it accompanies them to the bladder, assuming the proportions of an outer sheath, and thus running diagonally forward and downward through the fibrocellular inter-floor space, to right or left of the vagina. Here this sheath is attached by fibrous tissue connection in all directions, the best defined being towards pelvic wall, bladder and vagina. Similar condensations of tissue accompany all vessels going to and from the vagina, which means that such supports, for they are supports, are best defined laterally. A striking development of this nature accompanies the vessels of the bladder, as they leave the pelvic wall, and constitute a broad ligamentous structure, extending thence to top, to bottom, and to the lateral aspects of that viscus. Toward the base it extends so as to envelope that region well out toward the trigone.

If in connection with this description we recall the elongation all these lines of support suffer in prolapse, we realize the vital importance of an operation that will shorten them. An admirable illustration is furnished in the case cited, upon which the operation offered was performed.

Reference to the accompanying anatomical *Plate I* will help to explain the text. (The uterus and bladder are forcibly drawn upward.) The bladder is separated from the vagina as far as the trigone, the outline of the ureter is shown as it passes to the bladder. The broad ligament as far down as basic line is cut from uterus, the peritoneum is removed from the exposed region and with it the round ligament. The extension downward upon the vagina of a continuation of the broad ligament is shown also, together with the outward extension of this structure to and behind the ureteral sheath. The outer attachment of the basic line of broad ligament is drawn up to show how a similar structure (which encloses the cystic vessels), runs forward and inward to envelope the bladder and lend support to ureter and indirectly to the vagina. The tissue invoked in the suturing anterior to the uterus is that lying between the vagina and ureter, and also that which is above and beyond the ureter. The uterosacral ligaments are the only tissues involved in the operation that are behind the uterus. They are out of this field, the one on the right side is hidden behind the remnants of the broad ligament.

THE NEED FOR FURTHER DEVELOPMENT OF THE SURGERY OF THE UPPER PELVIC FLOOR BY DIRECT (SUPRAPUBIC) APPROACH.*

W. M. Polk, M.D.

I propose to illustrate this subject by reference to eleven cases of operation between January, 1909, and April 29, 1910, as follows:

One was a case of complete prolapse or procidentia. Two were cases of partial prolapse, the cervix resting at the ostium vagina. Five were cases of retroversion with adhesions, etc. Three cases of retroversion without adhesions, and one a case of

* Trans. Am. Gyn. Soc., 1909, p. 144.
Reprinted from the American Journal of Obstetrics and Diseases of Women and Children, vol. LXII., No. 4, 1910.

prolapse of the pelvic floor subsequent to a hysterectomy some years prior. None of the cases being little more than a year's duration (since operation) and some a few months at best, we must withhold conclusions as to ultimate results for some time yet. Meanwhile we can consider the operation, first as to its necessity, and second as to the manner of its performance.

The necessity for some such operation I believe to be conceded by a large majority of workers in gynecological surgery. The operation is based on the conception of the pelvic floor as a structure of double formation, with an outer or lower floor, made up of muscle and its encasing fascial coats, and an upper or peritoneo-fascial structure. The accessibility of the lower floor has enabled us to restore it—the inaccessibility of the upper has led us to indirect lines of approach, and to more or less incomplete or inadequate measures for its restoration, or to measures which lend to organs, needing support, the aid of suspension.

The men who forty years ago gave so much time to the pessary were fully alive to the needs of the situation, they had already largely solved the role of the pelvic floor, for on finding that repair of all parts then within reach gave incomplete results,

From Records of Bellevue Hospital.

Name.	Age.	Civil State.	Admitted.	Operated.	Diagnosis.	Discharged.	Results.
L. L.	35	Married..	Nov. 10	Nov. 15	Prolapse of uterus	Jan. 13	Exam. Apr. 5. Uterus in good position. Complains of pains in region of broad ligament; tenderness insignificant.
T. K.	35	Married..	Jan. 12	Jan. 14	Retroversion of uterus with adhesions	Feb. 5	Exam. Apr. 5. Uterus in good position; no indurations around organs.
M. B.	40	Married..	Jan. 25	Jan. 31	Retroversion of uterus	Feb. 23	Exam. Apr. 5. Uterus normal in size; slightly antiflexed. Induration around organs disappeared. Position ideal.
E. C.	25	Married..	Jan. 29	Jan. 31	Retroversion of uterus	Feb. 23	Exam. Apr. 5. Uterus in good position standing; drops to first position lying down.
M. McI.	26	Married..	Feb. 17	Feb. 18	Retroversion uteri with adhesions	Mar. 10	Uterus in good position; no tenderness; slight thickening about region of broad ligaments.
A. C.	28	Married..	Feb. 16	Mar. 4	Retroversion uteri	Mar. 23	Uterus in normal position. To return for observation.
M. D.	24	Married..	Mar. 18	April 1	Retroversion uteri with adhesions	April 22	Three weeks since operation. Uterus in good position. Some exudate and tenderness behind.
B. F.	25	Single....	April 4	April 11	Retroversion of uterus with adhesions		Case in ward now. Too early for report.
M. D.	38	Married..	April 25	April 29	Prolapse uteri with adhesions and chronic salpingitis		Case in ward now. Too early for report.
M. M.	50	Widow...	Nov. 18	Nov. 22	Prolapse of vagina and stump of cervix. Cystocele and rectocele	Feb. 10	Patient had a panhysterectomy in 1893. Tissues in pelvis indurated and adherent. Discharged improved.

they worked out the pessary and its mechanism. They called in additional uterine support. In reality a support to the upper pelvic floor, a further necessity in ptosis of the uterus.

Let any one on opening the lower abdomen of a normal nullipara, pass the right hand to the bottom of the pelvis, place the index and middle finger astride the broad ligament close to uterus, press them down until they rest upon the peritoneal reflections passing forward to the bladder and backward toward the sacrum. With the fingers of the left hand in vagina outline the levator ani muscle, especially as it passes to right and left of this canal, then press upward to contact with fingers of other hand. There is an intervening loose space and an upper plane of resistance. This is the upper floor and its main structure is the peritoneum. Between the muscle below and the peritoneum above is that area of cellular tissue so well known. Whence its embryonic origin we know not, its actual function is evi-

dent on any dissection. The condensations of this tissue along blood and lymph vessels and nerves, and along the ureter, its concentration about and attachment to the viscera it encompasses give it the same relative strength and importance that belongs to the mesentery, and what it undertakes to do for pelvic organs it adequately performs so long as it is in normal condition, and position.

The accidents of parturition and of genital infection all too often prevent this—so that in various ways it departs from its normal condition and position.

Suppose an antecedent relaxation of the pelvic tissues from inflammation or subinvolution; and I refer not merely to the subinvolution of pregnancy, but to that of menstruation as well. The woman stands, works, strains. Bear in mind that the attachment of the principal lines of condensed tissue, perivascular and ureteral referred to above, is from above downward, and from behind forward, following the outward or peripheral trend of the structures they envelop, the line of yielding of the floor is forward and downward, the lower segment of the uterus is swung forward and downward, the broad ligament holds the upper part backward, gradually the anterior face is turned upward, the intraabdominal pressure plays uninterruptedly upon it and retroversion is complete.

Such being the mechanism an operation must be devised to meet it.

We must work at the upper layer just as our predecessors did upon the lower. Knowing the shortcomings of the various plans of suspension we must abandon them and concentrate our minds on the fundamental aspect at the upper floor. We must not be deterred from the direct approach. We must realize how little shock is involved in work between bladder and uterus. We must work out the relative value of the supports through vessels and that from the peritoneum. (This latter not so much a support as an opponent of intraabdominal pressure.) So that we meet gravity by restoring the true supports, and intraabdominal pressure by taking up the slack in the peritoneal expansion upon pelvic floor.

As to the manner of performing the operation, on upper pelvic floor, from above, in cases of retroversion, it is merely a part of that already placed before you a year ago.

The need for preliminary treatment in all cases is imperative.

On page 144, Transactions of American Gynecological Society, 1909, is an illustrated article on the operative treatment of the prolapse of the uterus. The degree of prolapse represented in retroversion is, of course, far short of that represented in procidentia, but the operation for the one passes into that for the other, the two being but different phases of one condition.

The essential thing in both operations is exposure of the uterovesical region. Where the operation is to be as extended as a procidentia would call for, the coils of small intestine should be lifted from the pelvis and held back by means of gauze pads. The patient must be in the Trendelenburg posture. In procidentia more or less separation of the bladder from the vagina is necessary. In retroversion this is not the case. In retroversions the small intestines may or may not be removed from the pelvis, as the operator may determine; it being unnecessary if the space between the uterus and bladder can be kept cleared without it. The Trendelenburg posture may or may not be necessary, depending upon the case. As a rule, a shallow pelvis permits an operation more readily than a narrow and deep one. A moderate Trendelenburg posture is recommended. The intestines must be removed from the anterior pelvic culdesac, and held back by gauze pads. The peritoneum is slit longitudinally from the beginnings of its loose attachment on the anterior face of the uterus to its reflection upon the bladder. This peritoneum, with the immediate subjacent fascia, is then gently stripped back as far as the space just outside the vagina right and left. The uterus can now be caught between the thumb and two fingers (the thumb in front and the fingers thrust into the culdesac of Douglas) and drawn up into the opening. If the uterus cannot be seized as above described it is caught with a double tenaculum just above the uterovaginal junction in front and then drawn upward and backward. The lateral columns of the vagina are now brought together along the median line by three or four medium-sized sutures of kangaroo tendon. The first suture is placed about on the level of the external os or lowest point of the cervix. The last is placed just above the uterovaginal junction. They enter the cellular tissue just at the lateral vaginal wall, are buried in the outer portion of that wall, brought out about one-quarter of an inch from the point of entrance, pass off to the opposite side of the vagina, and are there entered and brought out into a position corresponding to the point of entry. The veins, of course, will be involved, but as the venous anastomosis is very extensive in this region, no inconvenience will follow. The uterine artery is easily averted by palpating it between the thumb and forefinger thrust down astride the corresponding broad ligament. The ureter is too far removed from the region involved

in the operation to cause embarrassment. Blunt dissection will quickly reveal the exact nature of the tissue included in the suturing. The effect of these three or four interruped sutures placed as designated will be to take up the slack in the lateral and posterior supports of the uterus and upper vagina, and in so doing meet the essential defect in cases of retroversion. The next step is to take up the slack in the peritoneal reflection between the bladder in front and the uterus and broad ligaments behind. This is done with chromicized catgut. The extent to which the peritoneum is drawn in toward the central line is governed by the amount of inward traction required to take up any slack which may remain after the subperitoneal sutures in the vagina have been tied. This inner traction of the peritoneum tends to draw the round ligaments and inner face of the broad ligaments inward. The question, therefore, has presented itself to me whether the slack in the peritoneum in the uterovesical fold above mentioned might not be better dealt with by shortening the round ligament. Such a step will take up a good part of the slack and perhaps it might be found a proper way to deal with this part of the problem. It has the advantage also of tilting forward the fundus where the uterine body is very soft, especially in such cases in which, owing to this softening, the uterus bends easily, and falls forward or backward, in response to any impetus it may receive.

In concluding let me emphasize the value of preliminary treatment in retroversion. In many instances, especially the unmarried presenting no symptoms, it needs no treatment; but when it does, curetting and associated care is most helpful, and in certain cases in which there is no change in position of lower segment of uterus (marked retroflexions) in most instances it is all that is needed.

THE SURGICAL TREATMENT OF POSTERIOR DISPLACEMENTS OF THE UTERUS.*

CHARLES CLIFFORD BARROWS, M.D.

In an active practice of gynæcology extending now over a period of almost twenty years, experience has shown me that displacements of the uterus, with the pathological conditions, dependent upon them, comprise a large share of the noninflammatory troubles peculiar to women. Of these displacements, those which result in a position of the uterine body posterior to that which it occupies in its normal state form much the larger share. Except in few instances, nonsurgical measures prove purely palliative, and in most instances are unsanitary and unsatisfactory.

My purpose in offering for your consideration to-night these personal experiences with the surgical treatment of posterior displacements of the uterus is to provoke, if possible, such a discussion as will illustrate the advantages of those operations which have proved satisfactory in your hands and mine, and to point out, if possible, some of the disadvantages and dangers of those procedures which have failed to meet with our approval.

In general medical and surgical gatherings such as compose the meetings of the Bellevue Alumni Society, a discussion of this character is of vastly more benefit than in a society composed entirely of gynæcologists. This is particularly so in this case, because in probably a majority of instances these patients come into other hands before they reach the office of the specialist. These men should be in a position to at least discuss with the consultant the advantages or disadvantages of any particular surgical procedure which he may suggest to the patient.

I shall not attempt to describe all or any great part of the many operations which have been put forth for the relief of this very common complaint. Some of them are good and safe, others are safe and inefficient, and others should demand the intervention of the police if suggested to an intelligent physician or patient—such for instance as that brutal and barbaric form of torture disguised under the name of operation, by Schuching. In this procedure, you remember, a needle concealed in a curved cannula and armed with a stout cord was introduced into the uterus and thrust through its anterior wall to return again into the vagina. The cord was then drawn through and tied in front, thus bending the uterine body upon itself anteriorly. At times the needle might pass through the bladder or again perhaps through a coil of intestine, but these "accidents" the author tells us were not very common. Could one conceive, possibly, of a more dreadful proceeding?

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It seems to me that the object of all surgical procedures in these cases should be to restore the uterus to a position as nearly possible to the normal and to maintain it there with comfort and safety to the patient, this, of course, carrying with it a relief of the symptoms from which the patient has been suffering.

I believe we can safely leave out of the question vaginal fixation and all those operations having this plan of approach for their base, since I think I am correct in saying that except in the hands of a very few surgeons they have been proved to be distinctly unsatisfactory

This brings us then, naturally, to the consideration of two distinct principles of procedure, the first having for its basis the artificial suspension or fixation of the uterus to the abdominal wall by means of inflammatory adhesions between that organ and the parietal peritonæum; the second depending for its success upon the restoration of the uterus to its correct position in the pelvis, and the maintaining of it there free from adhesions by utilizing its own natural supports.

Nature has been almost prodigal in its supply of ligaments to the uterus, since weight for weight, there are very many more such ligaments furnished this organ than any other organ in the human body. But the reason for this is very clear, since no other organ undergoes the enormous changes in size and position that the uterus does during the period of gestation. These supports are so constructed as to accommodate themselves to the changes taking place in their supported organ. This fact itself would lead us to turn to these natural means of support for a correction of the displacement, and by utilizing them leave the uterus in a position to undergo its changes without difficulty or danger.

In the study of all the cases of retroposition of the uterus that have come into my hands for operation, I must divide them into two simple groups: 1, hospital patients; 2, private patients. In the first group—that is, patients operated upon in the hospital—not private patients—296 cases. In the second group—private patients—102 cases, making a total of 398 cases.

The wisdom of this division for purposes of study can be easily understood when one comes to look up his hospital histories. The patients are discharged "cured," with careful instructions to report or return if the cure is not complete or permanent, and they disappear never to be seen again. This is particularly so, as we all know, of the class of patients coming to us in Bellevue Hospital, and it is there that by far the greater part of my operative work has been done. In attempting to draw conclusions from one's operative work it would plainly be unfair to assume that all of these patients were actually cured or relieved of their symptoms. We can only say that they left the hospital anatomically cured of the displacements.

But the 102 cases which come under the head of private patients furnish in themselves sufficient material for an intelligent study of the results obtained by me in my attempts to relieve posterior uterine displacements by surgical means. I have been able to follow closely practically all of these cases, and five of them have been under my obstetrical care subsequent to the operation for displacement.

Of the 398 cases demanding operation for posterior displacement of the uterus, 361 patients were subjected to some form of shortening of the round ligaments, and thirty-seven to some form of attachment of the uterus to the anterior abdominal wall. Of the 361 cases in which the round ligaments were made use of for the correction of the displacement and the maintenance of the organ in its normal position, the procedure devised by Mr. Alexander, of Liverpool, was employed in 302 cases. In fifty-one of these 302 cases the abdominal cavity was opened, either by an incision through the anterior abdominal wall, or by means of a posterior or anterior colpotomy. In fifty-nine cases the round ligaments were shortened within the peritoneal cavity, usually by means of the procedure suggested by Wylie, and in three instances by bringing two loops of the round ligaments together in front of the uterus and securing them there with sutures, as done some years ago by Polk.

In twenty-four cases the uterus was attached to the anterior abdominal wall, in a large majority of these a suspension being the result sought. In many of the cases in which this procedure was adopted, as well as in which internal shortening was the plan preferred, other intrapelvic work was demanded, such as the breaking up of adhesions, removal of tumors of the uterus or its appendages, conservative operations upon the uterine annexa, or the shelving of a displaced ovary.

I shall dismiss now the analysis of the total number of cases and confine myself to the 102 cases collected under the head of private patients.

Of these patients two have been the subject of suspension or fixation. Suspension was attempted, but in one patient at least, fixation seemed to be the result. In ten patients the ligaments have been shortened within the peritoneal cavity, four of these cases being in conjunction with the operation devised by me for shelving prolapsed

ovaries. In the other ninety patients the round ligaments were shortened by means of the Alexander operation. The two operations of ventrosuspension were done early in my experience. For more than ten years now I have not resorted to this operation, either in private or hospital practice. In one of the cases of ventrosuspension the patient seems to have complete relief of her symptoms, and the uterus remains in an apparently normal condition. In the second case pregnancy followed about one year after the operation. The patient was a multipara, having had two easy normal confinements prior to the operation. During the pregnancy she suffered unusually from dragging pains, and toward the latter part of the pregnancy almost constant pain in the costal regions. I did not see her during the latter months of her pregnancy, but was called after her labor pains had begun. The cervix was very high in the pelvis, having been carried upward and backward almost to the promontory of the sacrum. I finally delivered the child by version, with great difficulty. There was an extensive tear of the cervix, extending well up into the broad ligament. Convalescence was tedious, and extensive secondary operations were necessary. I determined then that this should be my last experience with this procedure.

In the ten cases of internal shortening I have had two relapses, the uterus within a few months finding its way back to its old retroverted position; so that this operation has not brought me the results that would impress me with its excellence.

In the ninety cases in which I have had occasion to resort to the Alexander operation, I have had one relapse, and with this an inguinal hernia, the only instance of this kind that has come under my observation. This patient—an artist's model—contrary to my instructions, went back to her arduous duties within two weeks of the date of her operation. At the end of two months she returned to me with as complete a retroversion as she had had in the beginning, and with a small, easily reducible, left indirect inguinal hernia. I opened the wounds again and found the attachment of the ligaments intact but the ligaments thinned out almost to a thread. I opened the inguinal canals, followed the round ligaments up and again shortened them in the usual manner, at the same time doing a radical herniotomy on the left side. She made an excellent recovery, and shortly afterward was married. She soon became pregnant and went to term with no unusual discomfort. She had a normal confinement and satisfactory recovery under the care of Dr. R. Ewell Brown.

I have had occasion to attend in labor four other women upon whom I had previously done the Alexander operation. In no case was there complication of any kind, the labors being satisfactory in every way. In one instance low forceps was applied to the head on the perinæum. This was a young married woman referred to me by Professor W. Gilman Thompson, because of sterility, where a posteriorly displaced uterus was doubless the cause. Following the Alexander operation she soon became pregnant, and was delivered, as reported. Her child is now six months old, and her uterus is in its normal position. So much for my own experience. Let us now consider the operations in themselves.

1. Operations depending for their success upon artificial adhesions between the uterus and the abdominal parietes. This operation, suggested by Olshausen and made practical and popular by Kelly, is, I believe I can safely say, resorted to more frequently for the relief of posterior displacements than all other operations combined. By the masterful force and the brilliant skill and earnest advocacy of its accomplished inventor, this operation has become, I believe I am safe in saying, a routine procedure at the hands of many gynæcologists and certainly of most general surgeons who do gynæcological work. And it is to these gentlemen largely that I desire to address myself to-night, because even in this city, and certainly outside of large medical centres, a large proportion of these cases fall into their hands.

The things to consider about this operation, as about all surgical procedures, are: A. Will it relieve the condition for which it is applied, and is the cure a permanent one? B. Does not the operation entail great risks to the patient?

In the consideration of the so-called suspension of the uterus, it seems fair to assume that the surgeon cannot depend upon definite results. Kelly says that in seventeen cases in his clinic, operated on at periods varying from ten months to three and one half years after a successful suspension, there was a single ligament in twelve cases, of varying lengths and thickness; in four cases two slender cords were found, and in one case there were three cords. Lynch reports two cases, the subjects of Cæsarean section, where suspension was attempted and fixation resulted. It does not seem unreasonable, therefore, to assume that the number, the length, and the size of the suspending cords are largely problematical, or that fixation may take place where suspension is intended.

This whole matter, it is readily seen, depends upon the extent and depth of the inflammatory process, which unites the peritoneal covering of the uterus to the parietal

peritonæum. This is a matter of chance—of good luck—rather than of scientific accuracy.

Goffe (in Bovée's Practice of Gynæcology), reports a case in which he operated four months after suspension of the uterus, in which that organ lay in the hollow of the sacrum, the lax bands or "ligaments" being four and one-half inches long. Through the kindness of Dr. Polk I am able to show you just such a band occurring in just such a case, which recently came into his hands for a second operation, the suspension having been done by a surgeon in Baltimore. It is quite possible also that a suspension by reason of an inflammatory action set up at the site of the attachment may become a fixation, a condition, I believe, that all are agreed is not to be desired. Such a condition is well described in one of five cases of Cæsarean section reported by Cragin (*Transactions of the American Gynaecological Society*, 1908):

Mrs. S., age twenty-six, birth No. 21,080. In October, 1902, a very able New York surgeon, realizing full well the obstetrical dangers of a ventrofixation, performed with great care a ventrosuspension for retroversion of the uterus. The patient was much benefited by the operation, and in March, 1903, about five months after the ventrosuspension, she became pregnant. On December 5, 1903, she was delivered by the writer after a very easy and rapid labor. Her first stage began with rupture of the membranes at 8 p. m., just as she was starting for the theatre. The baby was born at 10.30 p. m. The position was left occipitoanterior.

It was thought by the surgeon who performed the operation, by her attending physician, and by myself, that the ventrosuspension had been a marked success and that no obstetrical complication from it need longer be feared.

In June, 1907, patient became pregnant again, and on the evening of March 26, 1908, the writer was again called to deliver her. On examination, the following conditions were found: The cervix was high up posteriorly and with difficulty reached. The child lay transversely, and the anterior uterine wall was thickened. As no progress had been made on the following morning, she was taken to the Sloane Maternity Hospital and Cæsarean section performed by me soon after her arrival. The suspension band, which in the first postoperative pregnancy allowed such normal uterine development and such a normal delivery, had in this pregnancy become thick and unyielding; whether as a result of the puerperal involution at the former labor (the puerperium was afebrile), or as a result of the present pregnancy, I know not. The condition was that of a ventrofixation and a Cæsarean section was the positive indication.

There can be no question, then, that ventrosuspension is an uncertain procedure, both in its accomplishments and in its results. Not only does it fail at times to relieve the conditions for which it is employed, but on some occasions at least produces symptoms which may be extremely annoying to the patient. Irritability of the bladder is certainly a common accompaniment. More than ten years ago I pointed out, I believe, the correct explanation of this. The act of urination may be easily divided into three stages: 1. A positive voluntary act—starting the flow of urine; 2, a passive middle period, during which the urine continues to flow until the bladder is almost emptied; 3, a last positive bearing down effort, crowding the abdominal contents down on the bladder and thus forcing out the last few drachms of urine.

Now, when the uterus is fixed like a roof over the fundus of the bladder, this final act is of no avail, and a certain amount of residual urine remains in the bladder and is responsible for its irritability. This applies to all attachments of the uterus to the abdominal wall, suspensions, of course, being, primarily, fixations depending for the formation of the suspensory cords upon the stretching out of the adhesions between the uterine and parietal peritoneum.

I have had three patients come to me upon whom suspension had been done, all by competent surgeons, complaining of constant dragging pain in the hypogastrium, in addition to the urinary symptoms. One of these cases is of such interest that I shall report it briefly:

Case I—A. B. came under my care in Bellevue Hospital, with the following history: Prior to the time that she had been admitted to the German Hospital for the purpose of having an interval appendectomy done, she had never had any pain or discomfort referable to the uterus. Shortly after she left the hospital she began to suffer from dragging pain in the hypogastrium, irritability of the bladder, and marked dysmenorrhœa. Vaginal examination showed the uterus in its normal position, but with limited mobility, apparently due to some attachment to the abdominal wall. I showed this patient to the students of Cornell Medical College, in Professor Polk's clinic at Bellevue, as a case with ventrosuspension. On opening the abdomen it was seen that the appendix vermiformis had been removed and that the uterus had been suspended to the anterior abdominal wall. The suspensory cord—about one inch

long and as large as a large lead pencil—was removed. The patient was relieved promptly of her abdominal pain, her irritability of bladder, and her dysmenorrhœa, and reported to me a year after as being entirely well.

That this procedure entails grave risks to the patient in not a few cases, I believe its most ardent advocates will allow. From what has gone before I believe we must admit that it is impossible to predict, or at times distinguish between ventrosuspension and ventrofixation, and as pointed out by Cragin, suspensions at times become nxations and fixations suspensions.

Lynch reports twenty-five Cæsarean sections and Cragin adds five of his own, necessary because of this procedure, and I desire to report here a case of my own, occurring at the Manhattan Maternity, which should prove of interest in this connection.

Case II—The patient, A. D., a German woman, secundopara, aged twenty-four, was admitted to the Manhattan Maternity Hospital on April 8, 1907, in the first stage of labor. She gave no history of miscarriages. Her previous pregnancy was normal; a child was delivered stillborn instrumentally. The external examination showed a full term fœtus, head below, back to the left, shoulder presenting, left scapula anterior. Internal examination, old laceration of the perinæum, cervix retracted, three fingers dilated. Diagonal conjugate 10 cm., true conjugate 8 cm. Diagnosis: Simple flat pelvis, neglected shoulder presentation, patient in labor thirty-four hours before admission. Liquor amnii drained; hand prolapsed into vulva. Cæsarean section done by Dr. Barrows and a live child delivered; weight, 6 pounds 4 ounces. Resuscitation by combined method for twelve minutes. Left forearm showed marked contusions. Diameters of fœtal head—Biparietal, 8.3 cm.; subbregmatic, 9.3 cm.; occipital frontal, 10.7 cm. Puerperium uneventful except for slight stitch infection at the upper end of the incision. Examination at the time of discharge showed adhesions between the uterus and abdominal wall. The uterus was at the umbilicus.

This woman left the hospital in excellent condition with the exception of this adhesion, which had taken place between the anterior face of the uterus near its fundus, and the anterior abdominal wall. She was instructed that in case she should again become pregnant to report to us promptly.

On March 10, 1908, she returned to the hospital, telling us that a pregnancy had begun on July 23, 1908, fourteen and one-half months after her previous operation. Measurements at that time showed externally between the spines, 24 cm.; between the crests, 29 cm.; external conjunctiva, 17 cm.; right external oblique, 21.5 cm.; left external oblique, 21 cm.; diagonal conjunctiva, 10 cm.; transverse outlet, 8 cm.; posterior outlet, 9 cm.; true conjunctiva, 8 cm. Examination also showed a fœtus in the transverse position, head to the right dorsal plane below. The fœtus was easily movable. The position could readily be changed to breech or vertex presentation. The fœtal heart was heard clearly. The patient's general condition was good. The patient stated that for the past month or more she had suffered a great deal of pain and pulling, dragging sensation in the hypogastrium, and a severe painful pressure in the costal region. She was examined by me on April 7th. The conditions were found as noted, and on vaginal examination it was practically impossible to reach the cervix. The uterus had evidently developed posteriorly and carried the cervix high up, apparently above the promontory of the sacrum. It could be easily demonstrated that the uterus was attached to the anterior abdominal wall, but could be moved to a limited degree. The whole uterine tumor lay high in the abdominal cavity and was well up under the costal margins.

I advised the woman to return on April 13th, a week from the date of my examination, this being a week or ten days before she was due for delivery. I did a second Cæsarean section on April 14th and delivered her of a living child. The measurements of the child were: Biparietal, 9.5 cm.; subbregmatic, 10 cm.; occipital ment., 13 cm.; occipital front, 12 cm.

The woman was instructed to return, and an operation was done at this time a week or ten days prior to term, because I believed that the uterus in all probability had thinned out very much posteriorly, and that if any labor pains should begin, there would be great danger of rupture of the uterus. On opening the abdomen I found a band about one and a half inches long and as large as a large lead pencil, connecting the uterus just below a line between the origin of the Fallopian tubes with the anterior parietal peritonæum. This peritonæum on the parietal side was drawn out in a fanlike shape. The development of the uterus had occurred posteriorly, the uterus evidently rising in the pelvis as far as this connecting band would permit. Then the tension on the band had swung the uterus around so as to make a half torsion of its body, the left cornu and Fallopian tube presenting in the wound when the abdomen was opened, and the right one being well behind the uterine body as it lay in situ, as shown in Fig. 1.

The band was tied off and removed. The scar of the former section showed faintly along the anterior uterine wall (Fig. 1). The uterus was opened in the same line, it being found about two or three times the ordinary thickness of the uterine body toward the lower part of the incision (Fig. 2). The child was presenting as a breech and was easily delivered. The placenta was situated posteriorly near the fundus at a point where the uterus was thinnest, the uterine wall at this point being not more than one sixteenth of an inch thick (Fig. 2). This showed very clearly the wisdom of not permitting this woman to go to term, as any uterine contraction might, in all probability, have produced a rupture of the organ.

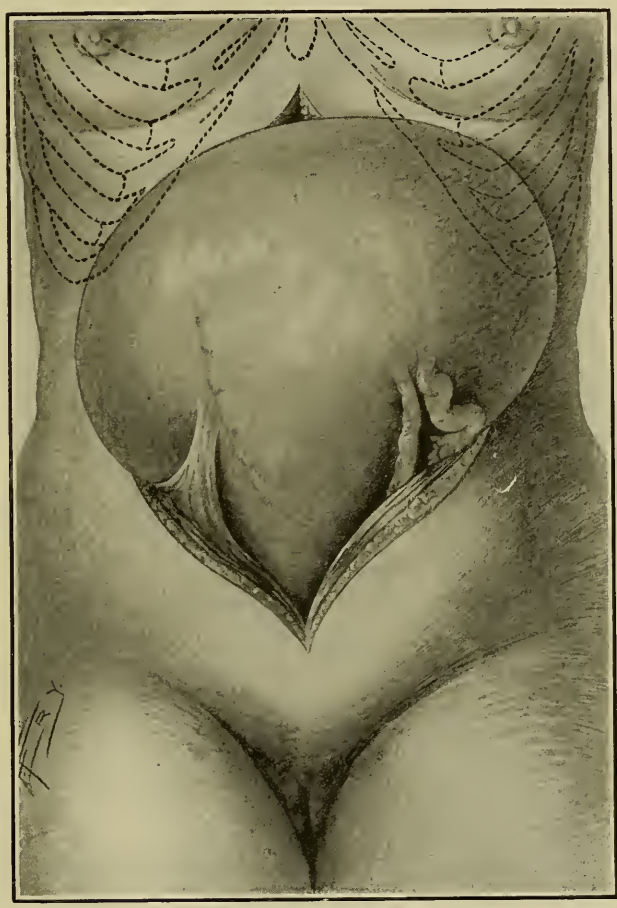

Fig. 1.—Band connecting abdominal wall and uterus at site of former incision. Half torsion of uterus.

The woman made an uneventful recovery and left the hospital well. We have tried to impress upon her the necessity of returning to us immediately in case she should again become pregnant.

This accidental ventrosuspension was as perfect a one as could have been done intentionally. It is the only one that I have done for a long time, and I regret that I was unwittingly the indirect cause of this. With the pelvic measurements a little below the normal I believed that a viable child could be delivered through the natural ways, and for that reason I had instructed this woman to return to us early in her pregnancy, if it should occur, in order that we might take measures to accomplish this result. When she did return, she had passed the point where it would have been possible to have delivered her through the natural channels. As I have said before the cervix had been carried up so high and so far backward that the presenting

part could not be felt. The uterus was so high in the pelvis, and there was such a mass of thickened anterior uterine wall in front of the child, that it was clearly a case for a second Cæsarean operation.

Von Gerhard, Dickinson, Brodhead, Clark and Bowley, and Edebohls and Ingalls have all reported cases of rupture of the uterus during labor because of the thinning of the uterine wall behind the point of suture attachment. Dr. R. Condit Eddy re-

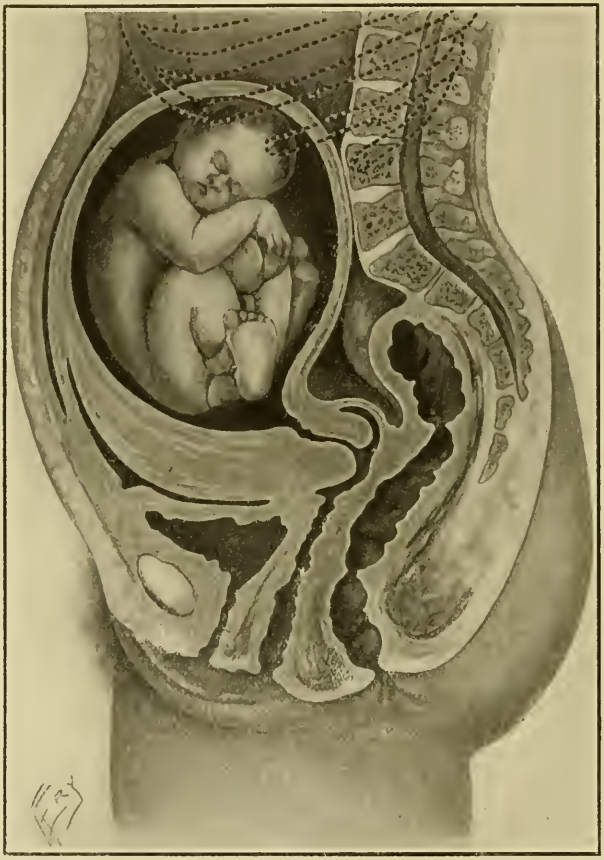

Fig. 2.—Thickening of anterior segment and thinning of posterior segment of uterus. Cervix abnormally high.

ported such a case to me as occurring in a hospital in a neighboring town while he was in attendance in the same hospital upon a patient in an easy labor, upon whom I had previously performed the Alexander operation. The patient was brought into the hospital dying from a rupture of the uterus. She had been easily and successfully delivered of five children prior to the suturing of her uterus to the abdominal peritonæum, and she lost her life in the first labor following that operation. Two cases of rupture of the uterus following suspension have been reported to me by Dr. A. A. Moore.

I believe then that we may safely assume that ventro-suspension is an unsafe operation for posterior displacements during the child bearing age.

A malposition of the child is the rule in those cases where Cæsarean section has been done under these conditions. In fifteen of the twenty-one cases reported by Lynch, and in all five of Cragin's cases transverse presentations were found; in my own one a breech.

In this connection it is an interesting study to see at what age women apply for operative relief from posterior displacements. In 456 cases collected from the reports

of Dr. Polk's service at Bellevue I find that ninety-six per cent. of the patients were below the age of forty, and that the average age was less than thirty-one. In my own cases forty-two years was the oldest age of 398 patients, and the average age was less than thirty; so that practically all patients who seek surgical relief from posterior displacements are of the child bearing age. If we look no farther than this, the cases to which this operation can be offered with assurance of safety are very few.

But it carries with it another danger which even the few who escape the child bearing age limit are not safe from. Nature is extremely careful in her plan of procedure within the peritoneal cavity, in the adjustment of the organs and viscera, and their fixation by ligaments, never to leave free bands under which or apertures through which coils of intestine may pass and go on to strangulation. All these have been so cleverly covered with the enveloping peritoneal membrane as to practically make intraperitoneal strangulation impossible. Such is not so when adhesions have

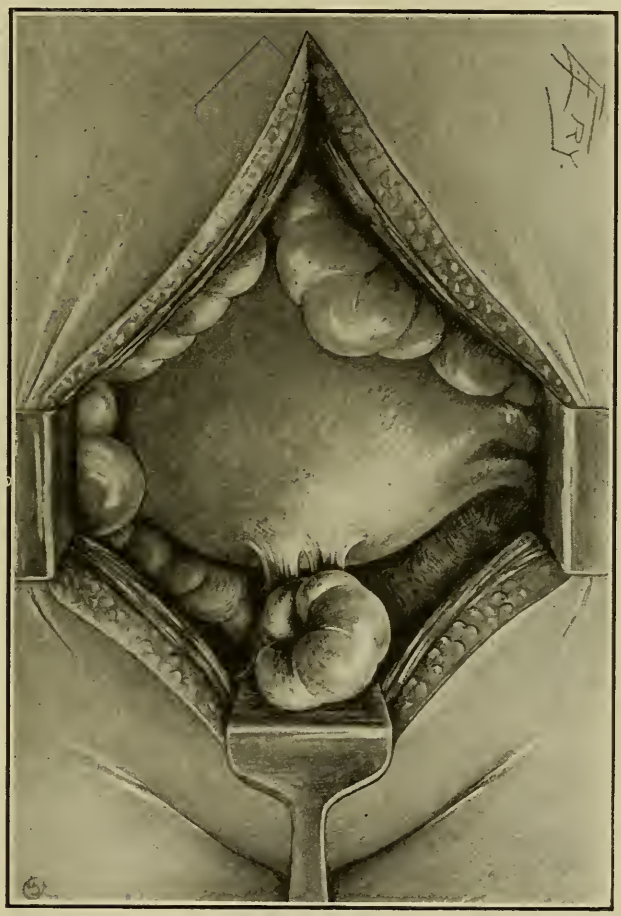

Fig. 3.—Coil of small intestine strangulated between bands of suspended uterus.

taken place and artificial bands and cords have been developed. Fatal cases of strangulation of the intestine following ventrosuspension have been reported by Lindfors, Jacobi, Ohlshausen, and Montgomery. In this connection the following case is of interest:

Case III—Mrs. M., age thirty-two, secundopara, referred to me by Dr. Bullard, of Larchmont Manor. About one year before I was called to see the patient she

had had a laparotomy done by a prominent New York general surgeon, who, it was said, had done some conservative operation on one tube and ovary, and at the same time had done Kelly's operation for ventrosuspension of the uterus. She had not had much relief following the operation, but was able to be up and about and attend in a way to her household and social duties. The day before I was called to see her she had been suddenly seized with a severe pain low down in her hypogastrium. This was accompanied by nausea and vomiting, with inability to secure a satisfactory movement of the bowels. Her abdomen was immediately opened and the condition shown in the sketch found (see Fig. 3). A knuckle of small intestine had slipped

Fig. 4.—Shortening of round ligaments, showing slender first portion and thicker and stronger portion deeper.

under one band of a ventrosuspension and passing up between the two cords had become partially strangulated. The gut was deeply congested but not yet gangrenous. The cords were cut, the gut liberated, and the abdomen closed. The patient made a good recovery, and is to-day—a year after the operation—well. If it had not been for the possibility of prompt surgical relief she would have been added to the list of fatal cases.

Now let us consider ventrosuspension as far as the effect on the symptoms and results to the patient go. Kelly, in his Operative Gynæcology, quoting Dr. Holden, says that "109 out of 182 women were absolutely cured or their symptoms were greatly relieved," that is, sixty per cent. of these patients as quoted by Dr. Kelly showed either cure or great relief; forty patients, or twenty-one per cent., had no relief; and the remaining thirty-three patients out of 182 cases were but slightly improved.

When we consider the possible disastrous results I have just tried to demonstrate to you and then look at the comparatively unsatisfactory conditions dependent on this operation, quoting as I have from Kelly, himself the author and strongest advocate of the procedure, it seems to me that it is a very poor return to offer to the patient when we can only promise about half the cases as cured or relieved, and when we have, on the other hand, the array of dangers and disasters which I have cited.

I am prepared to say, therefore, after a careful study of the literature of the subject and from my own personal experience, that at no time is ventrosuspension a procedure which we can offer to the patient with safety and satisfaction.

Let me say that since 1895 (about fourteen years), in the gynæcological service in Bellevue Hospital, of which Dr. Polk is chief, only eight ventrosuspensions have been done. Of these, six have been done by general surgeons who have had charge of

the service at times in the summer months during the absence of Dr. Polk, Dr. Hamlen, and myself.

Now let us consider those cases which come under a second caption, suspension of the uterus by means of its own ligaments, and for the sake of brevity, I will confine myself to shortening of the round ligaments by one method or another. If we expose the internal inguinal ring and draw the round ligaments out through the canal, in a large number of cases we will find that about the first half of the ligaments that is drawn out is slender and sometimes fragile, and easily broken if care is not taken in its handling. As the ligament is further drawn out, it becomes thicker and stronger and shows more clearly its muscular origin. I preface my remarks with this because the success of a correction of posterior displacement of the uterus by shortening these ligaments depends largely on this fact. When the abdominal cavity has been opened and the uterus is found in a retroverted condition, such operations as those advised by Wylie and others for internal shortening of the ligaments appeal to one on account of their simplicity, ease of execution, and apparent anatomical correctness, but the fact mentioned that the ligaments are thinned toward their outer extremity and thicker at their uterine end, brings about in this operation the removal of the strong part of the ligament by its inclusion in the loop, and leaves the weak part to serve as a supporting cord. For this reason I have not made use of internal shortening of the round ligaments when it was possible to resort to the procedure by Mr. Alexander.

Many objections have been offered to Alexander's operation. Some have said that it was a difficult procedure. I can answer this by saying boldly that it is not a difficult procedure to any person who knows the anatomy of these parts, and who has fair surgical skill. I have on many occasions exposed and drawn out both of these ligaments safely and without hurry in less than five minutes, and I have seen house gynæcologists at Bellevue Hospital frequently do practically the same thing. In the 296 cases to which this procedure has been applied by me, I have never failed to find the ligaments in their proper position. To my mind they are as fixed and well established anatomical structures as the uterus itself, because they are prolonga-

Fig. 5.—Prolapse of ovary due to elongation of the mesovarium.

tions of the muscular structure of the uterus, from its cornua along the top of the broad ligament and through the inguinal canals. At times I have found these ligaments so thin and fragile that I have been obliged to slit up the wall of the inguinal canal and follow them carefully until I came up to a thickened portion of the ligament, lying within the peritoneal cavity. On several occasions I have broken one ligament, but by entering the peritoneal cavity through the internal abdominal ring after the manner of Goldspohn, I have found no difficulty in securing the broken end. When the ligament breaks—and it ought never to break in the hands of a good surgeon—the rupture takes place in the thin outer part of it and not in the thickened uterine end. In the ninety cases which I have reported, outside of the one in which the relapse and hernia occurred and which has already been cited, I have had one complete failure anatomically. The uterus now occupies the same position which it did before the operation, but strange to say the patient has no symptoms and declares herself as well, and I have been unable to get her to submit to a second operation. In three of the cases my patients complain of discomfort and pain of a dragging nature, but the uterus occupies a correct anatomical position. Subtracting these four cases from the ninety cases occurring in my private practice leaves me eighty-six

cases, the patients in which I can safely say are cured. None of these cases are less than a year old, so that there has been fair time to test the question of relapse.

Now, I am quite conversant with the fact that these results are not such as are commonly believed to exist after operation, and I believe that such a good percentage of recoveries depends upon the great pains and care taken in the diagnosis of this condition. This operation should only be applied to those cases for which it is suitable. It is easy to see that if there are adhesions behind the uterus holding it in a fixed retroverted position, to draw out the ligament and make tension on the uterus in a forward direction would only add to the woman's discomfort, and yet this is one of the reasons why this operation has failed in the hands of a good many. We can also easily understand that if the woman has, in addition to her retrodisplacement, inflammation of her tubes or ovaries, or other pelvic inflammations, her symptoms are not relieved by restoring the uterus to its normal position.

Again—a condition exists in many of these cases of retrodisplacement which is not recognized by many gynæcologists and surgeons and indeed is said by many not to exist—namely, prolapse of one or both ovaries. When this prolapse of the ovaries depends simply upon their being carried backward and downward by the backward

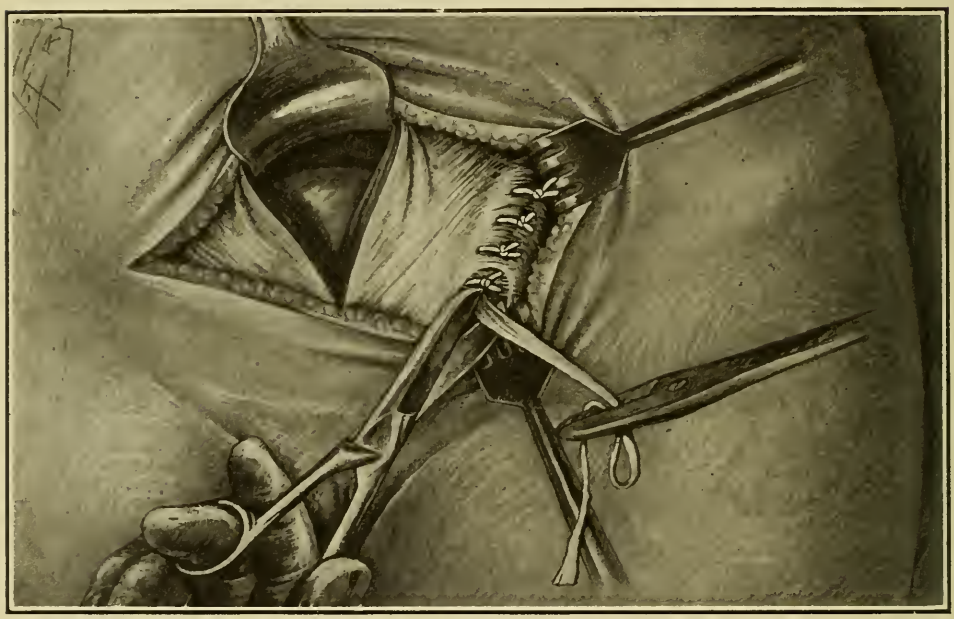

Fig. 6.—Removal of excess of ligaments after shortening. Abdominal cavity and external inguinal ring exposed by single incision.

displacement of the uterus, a restoration of the uterus to its proper position will carry with it a relief of the displacement of the ovaries; but in a large proportion of cases such as I have described in an article published in the *Medical Record* some ten years ago, ovaries are frequently prolapsed because of the elongation of the mesovarium or fold of peritonæum which holds the ovary against the posterior face of the broad ligament (Fig. 5). It can be easily understood if this occurs, elevation of the uterus in no way corrects a displacement of the ovary.

Then, again, I have found of late that in a fair proportion of posterior displacements of the uterus we have an enlargement of the veins of the pampiniform plexus to such an extent as to produce a condition analogous to that of varicocele in the male. Restoration of the uterus to its normal position in these cases relieves in a measure the congestion which exists in these veins, but it does not cure the dilatation of the veins, and they still remain a source of discomfort to many patients.

Such cases as these on which Alexander's operation has been done without a thorough investigation in advance of the existing conditions have been frequently set down as failures of the operation.

I think that the success of the operation also depends largely upon technique, and the technique devised by Mr. Alexander, himself, I am free to confess seems to me as nearly perfect as one could wish for, with one single exception, and this does not apply absolutely to his suggestions because he leaves you a choice of two methods. The exception lies in the disposal of that portion of the round ligament which has been drawn out. He in some cases removed this, but he tells you that if you choose to do it, you can tuck this into the wound and leave it there. Now, when we consider the fact that we have torn this muscular structure from its bed, and in doing so we have handled it more or less and broken up its nervous and vascular supply, and in addition to that, when we come to fix it and leave behind a portion which has no connection, practically having been shut off from the other part of the ligament by our sutures, I cannot find any excuse for not removing this, because it seems to me that it may act as a foreign body and result in a failure of the wound to close by primary union (Fig. 6).

Primary union is absolutely necessary for the success of the operation, as you can readily see that suppuration at the point where the ligament is attached will, in all probability, result in a failure to fix the structure firmly. If there is any question about the presence of adhesions or of other intrapelvic difficulties besides the displacement of the uterus, it is a wise thing to follow the plan suggested by Dr. Polk, twenty years ago, to open the abdomen from above, correct these conditions, and then do a secondary shortening of the ligaments. It was customary at that time to resort to some intrapelvic method of shortening the ligaments, but more than twenty years ago I have seen Dr. Polk open the abdomen, break up adhesions, close the median abdominal incision, and restore the uterus to its position by shortening the round ligaments after the Alexander method.

Of late I have been using the transverse (Pfahnenstiel) incision, from a point about one inch above the spines of the pubic. A transverse incision is made, the skin is drawn upward by retractors, and the abdomen opened in a median line. This is well portrayed in an article published by Peterson, of Ann Arbor, on Shortening the Round Ligaments within the Inguinal Canals through a Single Suprapubic Transverse or Median Longitudinal Incision, in Surgery, Gynæcology, and Obstetrics, July, 1906. This is a very satisfactory method of reaching the peritoneal cavity, and at the same time the external inguinal rings, through a single incision of no great extent (Fig. 6).

In closing this paper let me ask your forgiveness for having presented it in such a general way, but the subject is such a large one that I have found it difficult to confine myself within the necessary time limit.

THE ANATOMICAL BASIS FOR SUCCESSFUL REPAIR OF THE FEMALE PELVIC OUTLET.*

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The female pelvic outlet is subject to severe traumatism at every parturition.

Such traumatism may produce no more lasting effect than a ruptured fourchette or it may result in a tear so extensive as to sever all the tissues between the vagina and the rectum.

For years surgeons have been operating upon these lesions with varying success.

Any plastic operation to be successful must have a solid anatomical basis. Note, for instance, the great variety of operations proposed and practised upon the inguinal region for hernia and their indifferent success or complete failure until the procedure of Bassini was given publicity when a great gain in cures followed. Why? Because Bassini's operation has a solid anatomical basis for its execution.

It seems to me that the one *fundamental idea*, the only *rational aim* for the surgeon in all such plastic work is to *restore* the *damaged parts* to *their normal state;*

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in other words to follow Nature's plan in the reformation of the region under his consideration.

My purpose here is to demonstrate by actual specimens the structures which close the pelvic outlet in the female, to explain their action, to show what may occur if these structures are ruptured and to point out what seems to me, at least, the rational method for restoring these parts to a normal condition after such rupture.

I wish to state at the outset that I bring you nothing original. The anatomy of the part is the same as it has doubtless been for ages. The location and extent of the various lesions have been fully described by preceding writers. But the significance of such lesions is not universally recognized and their treatment varies almost with each individual operator.

In fact, the treatment of pelvic lacerations is in sufficient chaos to justify a reasonably careful review of the salient features of the subject.

I. The Anatomy of the Female Pelvic Outlet.

In this consideration I aim to point out only those facts which are pertinent to the practical aspect of the subject.

The Pelvis—The ossa innominata and the sacrum (with the coccyx) form the bony frame-work of the pelvic outlet.

It is an irregular-shaped segment of a cone to the upper border of which is attached the spine and the abdominal walls; to its lower and outer surface, the lower extremities, and about its inside, the structures which close the pelvic outlet.

Fig. 1.—The outlet of a female pelvis.

The Pelvic Muscles and Fasciae—The inner surface of the pelvis is padded by the obturator internus and the pyriformis muscles. Over these muscles is spread the pelvic fascia which forms a funnel-shaped membrane attached to bone and ligament about the margin of the muscles. Above, to the promontory of the sacrum, the iliopectineal line and the inner surface of the pubis. Below, to the ischiopubic rami, the tuberosity of the ischium and the great sacrosciatic ligament. The pelvic fascia is crossed from the inner surface of the pubis to the spine of the ischium by the "white line," which serves to mark the separation between the pelvic cavity above and the ischio-rectal fossa below. The pelvic fascia above this line is the *parietal pelvic fascia* and that below is the *visceral pelvic fascia*. The latter drops downward and inward to the bladder, vagina and rectum, forming for these viscera their true ligaments. The portion of the fascia over the obturator muscle is also called the obturator fascia, and that covering the pyriformis muscle, the pyriformis fascia.

The above statements agree with those given in the text-books of anatomy. Close dissection shows, however, that they should be modified in some particulars, for the following arrangement prevails in many of the female pelves.

If the anal fascia has been removed and the lower surface of the levator ani exposed, by gently using the fingers or the handle of a scalpel, it will be found that the levator ani and the parietal pelvic fascia are easily separated as one layer from a more external layer of fascia, which is the "true" obturator fascia. This layer covers

Fig. 2.—The left half of a female pelvis to show the line of attachment of the pelvic fascia, triangular ligament and the points between which the "white line" extends.

the obturator muscle and is attached to bone and ligament all about its margin, viz., along the iliopectineal line, to the upper margin of the obturator groove and to the inner surface of the pubis; below, to the spine of the ischium, to the great sacrosciatic ligament, tuberosity of the ischium and the ischiopubic ramus.

The inner layer is the parietal pelvic fascia, which for its upper attachment follows the same lines as the true obturator fascia does, but, after the limits of the

obturator muscle are passed, extends over the pyriformis muscle as the pyriformis fascia, and is in this region attached to the posterior portion of the iliopectineal line, the front of the sacrum, the great sacrosciatic ligament, and the spine of the ischium.

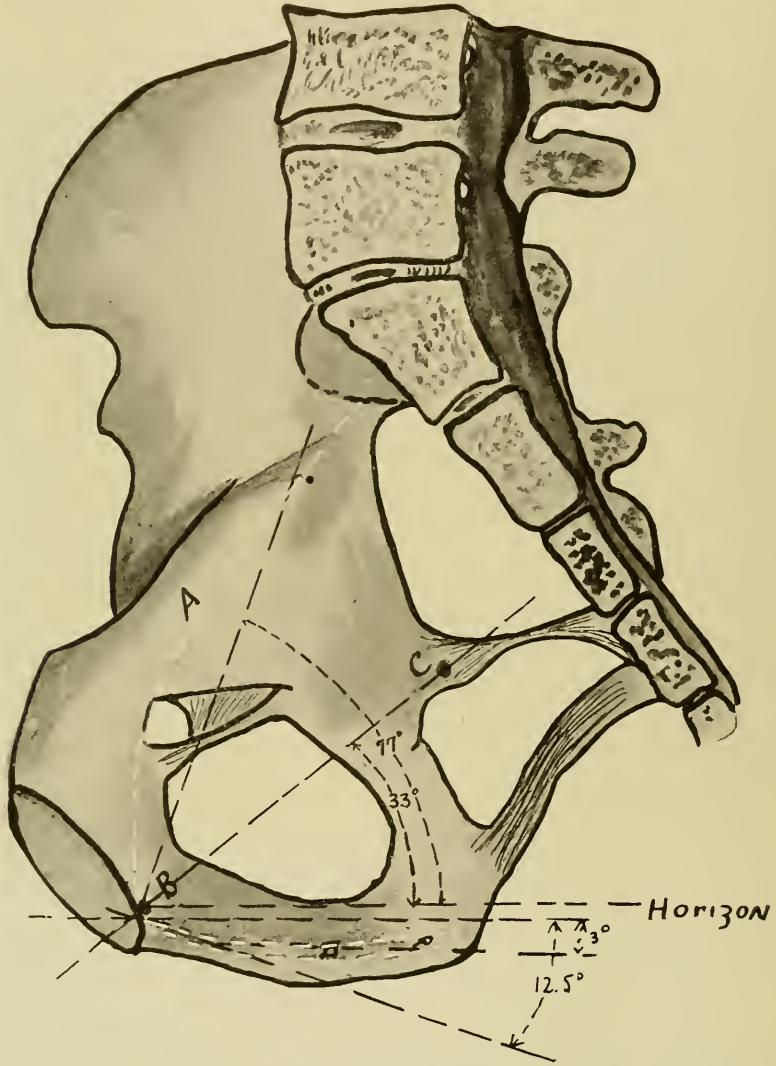

Fig. 3.—A side view of the right half of a female pelvis, placed in the normal position with reference to the horizontal plane. A, the line of attachment of the parietal pelvic fascia. The segment from A to B also indicates the attachment of the true obturator fascia; B the inner surface of the pubes, the beginning of the "white line," the origin of the pubo-coccygeal (pubo-rectal) portion of the levator ani muscle; C the spine of the ischium and the posterior point of attachment of the "white line"; D is placed between the attachments of the two layers of the triangular ligament (perineal shelf). It also indicates the lower line of attachment of the true obturator fascia. The angles that the various "lines" make with the horizon are indicated. Note that the perineal shelf is practically horizontal.

This fascial plane drops downward and is called the parietal pelvic fascia until a point is reached where it is thickened by the addition of some fibers running antero-posteriorly from the inner surface of the pubis to the spine of the ischium, the so-

called "white line"; below this line the fascia is called the visceral pelvic fascia, and it is disposed as previously given. There is thus formed a *continuous* plane or layer of fascia, the upper part of which is usually described as the parietal pelvic fascia and the lower portion as the visceral pelvic fascia, but the two portions are really continuous with each other without any mark of separation except for the thickening at the "white line," *but they are separated* from the true obturator fascia. The origin, then, as usually given for the parietal pelvic fascia is really the origin for the visceral layer of the same as well.

The Levator Ani (*and Coccygeus*)—The levator ani shows two distinct portions, the ilio-coccygeus and the pubo-coccygeus (pubo-rectalis).

The ilio-coccygeus is the portion arising from the "white line." It is inserted into the side of the rectum, the ano-coccygeal raphe or ligament and the coccyx.

The pubo-coccygeus (pubo-rectalis) arises from the inner surface of the pubis, passes backward alongside of the vagina to be inserted into the tendinous center of the perineum; and, sweeping around the rectum, it terminates in the ano-coccygeal

Fig. 4.—Dissection of the female pelvic outlet. Note the prominent pubo-coccygeal hammock formed by the sphincter ani externus and the sphincter vaginæ. Laterally is seen the levator ani muscle. Anteriorly is the perineal shelf, with the fibers of the transversus perinei muscle. The intimate intermingling of the sphincter ani externus and the sphincter vaginæ at the perineal center is well shown, indicating that these two muscles really constitute a strong muscular sling between the pubic arch and the coccyx.

ligament and coccyx. This portion of the muscle deserves further notice. Its fibers form a strong band (about three-eighths of an inch wide), which hugs the vaginal orifice very closely (forming the lateral compressor of the vagina), and is inserted in a "Y-shaped" manner. One leg of the "Y" terminates in the central tendon of the perineum, the other leg of the "Y" encircles the rectum and ends in the ano-coccygeal ligament.

The coccygeus muscle is relatively unimportant in this consideration. It arises from the spine of the ischium and the adjacent obturator fascia and lesser sacrosciatic ligament, it is inserted into the side of the coccyx and the lower end of the sacrum. The above statements are in conformity with the text-books. We find, however, they should be somewhat changed to agree with our dissections of the female subject.

The fascia of the pelvis being arranged in two layers as just given, the "true" obturator fascia and the parietal pelvic fascia, the origin of the levator ani muscle should be given in conformity with the dissections, namely, its *origin* is from the *outer surface* of the *parietal pelvic fascia above* the "white line." Some fibers of

Fig. 5.—Saggital section of a female pelvis. A nullipara, eighteen years of age, injected and hardened in formaline then frozen and cut in the frozen state. The bladder was well filled when the section was made and has since partially collapsed. The uterus was crowded backward by the bladder until its long axis was vertical.

Note the almost vertical course of the vagina; the almost horizontal course of the anal canal, and the right-angle formed between it and the rectum. The shape and relations of the ano-coccygeal and perineal bodies can be easily appreciated.

the anterior portion of the muscle even extend to the margin of the obturator groove and the iliopectineal line. This distinction is possibly without importance, except that it conforms to the usual findings at dissection. The result of this arrangement, then, is to make the *parietal pelvic fascia* really the *tendon* of *origin* for the levator ani muscle. So far as I can determine, the "white line" is *not* usually the *point* of *origin* for the *levator ani, neither* is it the place "along which the pelvic parietal fascia splits into the visceral pelvic fascia and the obturator fascia, neither does it give origin to the anal fascia" (see later). The "white line" is merely a thickening of the pelvic fascia along a narrow tract from the inner surface of the pubis to the spine of the ischium for the purpose of reinforcing the fascia at this place and unquestionably taking up much of the strain of the pelvic load and swinging it between the two bony points just named.

The Anal Fascia—The anal fascia is usually described as a thin layer covering the lower surface of the levator ani muscle and arising from the obturator fascia immediately beneath the "white line." As a matter of fact, this fascia is usually a well-marked one, or if thin in places has several dense portions in it, and, while it arises from the "true" obturator fascia (and not from the parietal pelvic fascia), this origin may be half an inch or more (sometimes almost as low as Alcock's canal for the internal pudic vessels) below the level of the "white line." With a low origin the anal fascia may blend laterally (as well as mesially) with the deep layer of the triangular ligament. If it has a higher origin, there is left a triangular osteofibrous space between the anal fascia, deep layer of the triangular ligament and the ramus of the pubes and ischium which is filled with fat. There is always a considerable quantity of fat interposed between the levator muscle and the anal fascia along their outer portions, but mesially the two structures become intimately blended about the perineal center and the rectum. *These three structures*, the visceral pelvic fascia, the levator ani muscle and the anal fascia *form* the *pelvic diaphragm*. Whatever concerns one affects all three. While they may be separately dissected and demonstrated along their lines of origin, at their insertion they become so intimately interwoven with each other that it is no longer possible to demonstrate them as separate layers without severing their interlocking fibers, and forming artificial planes of cleavage. This intermingling of fibers forms posteriorly the strong ano-coccygeal raphe, or ligament, centrally they assist in building up a dense fibromuscular mass between the rectum and the vagina, the "perineal body," and passing into the rectum and vagina they strengthen and thicken their walls (the rectum more than the vagina).

The Perineal shelf—This partial partition at the front of the pelvic outlet is formed by the two layers of the triangular ligament between which is inclosed the compressor urethræ (or vaginæ) muscle. These structures are attached laterally to the ischiopubic rami and the ischial tuberosities. Mesially, the superior or deep layer of the triangular ligament blends with the visceral pelvic fascia, the anal fascia and with the other fibro-muscular elements of the perineal center. The compressor urethræ (vaginæ) muscle with the fibers of the deep transversus perinei forms a muscular layer extending transversely across the subpubic space from one ischiopubic ramus to the other. These fibers pass behind (deep transversus perinei), and in front of the vagina (compressor vaginæ), and the anterior fibers surround the urethra (compressor urethræ). The inferior or superficial layer of the triangular ligament is similar to the deep one in its bony attachments. Posteriorly, it blends with the deep layer, with Colle's fascia and with the central tendon of the perineum. These layers of the triangular ligament with the intervening muscle close up the anterior or perineal portion of the pelvic outlet, forming a strong but dilatable plane horizontally disposed, which I should like to speak of as the perineal shelf, in order to drop lengthy descriptive terms and at the same time convey some idea of its function. The perineal shelf is pierced by the vagina and the urethra and some minor structures which do not require mention.

The Pubo-coccygeal Hammock—By this term I wish to group together parts which are usually described and considered separately, but which are very closely related anatomically and functionally.

The pubo-coccygeal hammock is formed by the sphincter ani externus and the sphincter vaginæ which, stretching from the pubis to the coccyx, form a veritable muscular hammock surrounding, closing and supporting the lower portions of the rectum (anus) and vagina. Separately considered, these muscles are disposed as follows:

The sphincter vaginæ has its interior attachment into the crura and base of the clitoris and into the subpubic ligament and the adjacent pubic arch; its posterior attachment is into the central perineal tendon. The sphincter ani arises from the tip and sides of the coccyx and the ano-coccygeal ligament, its anterior disposition is into the central perineal tendon also. The central attachment of these muscles deserves

Fig. 6.—Saggital section of the pelvis of a female subject, a nullipara, about seventy years of age. Hardened in formaline, frozen and cut in the frozen state. Small squares of paper were pinned over the subpubic arch and the tip of the coccyx, also a strip of paper was placed within the vagina to make its lumen more apparent, as the two walls were in such close contact they did not differentiate readily. Among other things, note the shape, position and relations of the bladder; the position and course of the urethra; the course and relations of the vagina; the horizontal course of the anal canal, and the less-than-a-right-angle formed between the anal canal and the rectum; the size and shape of the ano-coccygeal and perineal bodies; and the very much atrophied uterus, in a normal anteflexed and anteverted position.

a more detailed statement. We find here the fibers of the two sphincters intimately blending with each other and, also, with the fibers of the two transversus perinei forming an interlacement of muscular and tendinous fibers which with those just mentioned from the levator muscle and its fasciæ and the structures of the triangular ligament, produces a mass of muscular and fibrous tissue which is described as the "perineal body." It is placed between the anus and the vaginal orifice, where it measures one and five-eighths of an inch in an anteroposterior direction and extends upward for one inch between the anal and the vagina.

The anterior fibers of the sphincter ani spread out fan-shaped and terminate not only as given above, but also by being attached to the superficial layer of the triangular ligament. It requires no stretch of fact or fancy to conclude that this ligament answers as the tendon of insertion for a portion, at least of this muscle.

The pubo-coccygeal hammock is anchored and supported laterally to a small extent by the comparatively weak superficial transversus perinei muscles. These pass

Fig. 7.—Dissection of the female perineum. A, the pubis; B, the ischiopubic ramus; C, the ischial tuberosity; D, the great sacrosciatic ligament; E, the external urinary meatus; F, the orifice of the vagina; G, the tendinous center of the perineum; H, the anus; K is placed on the levator ani muscle and in the ischiorectal fossa; I, the perineal shelf. Upon it lie the superficial perineal vessels and nerves and the sphincter vaginæ muscle.

between the central perineal tendon outward and backward to the ramus and tuberosity of the ischium.

II. The Function of the Foregoing Structures.

The first statement I wish to emphasize is that while the various structures participating in the closure of the pelvic outlet have their own particular function, in their action, one cannot be considered alone and separate from the other elements. They all act in harmony and all to the same end, namely, for the preservation of the integrity of the pelvic outlet and in maintaining intraabdominal pressure, whether it be in micturition, defecation, copulation or parturition; or in resisting the increased action of the abdominal muscles and the diaphragm in various other bodily functions, as vomiting, coughing, sneezing and the like.

These features of the subject should be kept in mind:

1. The pelvic outlet is closed by a diaphragm formed of three intimately related structures: the visceral pelvic fascia, the levator ani muscle and the anal fascia.

2. The anterior portion of the outlet is further reinforced by the perineal shelf, composed of the two layers of the triangular ligament inclosing between them the compressor urethræ (vaginæ) muscle.

3. Lastly, there is the pubo-coccygeal hammock formed by the sphincter ani externus, sphincter vaginæ and the transversus perinei muscles.

These in whole or part are traversed by the urethra, vagina and anal canal and by other structures not pertinent to our consideration.

Fig. 8.—Dissection of the levator ani muscle, especially the pubo-coccygeal (pubo-rectal) portion with its "Y-shaped" insertion into the perineal center and the ano-coccygeal ligament. A. The symphysis pubis; B, the tuberosity of the ischium; C, opposite the vaginal orifice just above the metal hook; D, the tendinous center of the perineum; E, opposite the anus; F, opposite the coccyx; between F and E is the sphincter ani externus; between F and B is the great sacrosciatic ligament; in the centre of the picture is the ilio-coccygeal.

What is the mechanism by which they sustain the pelvic load? We may note that if the female went on all fours and did not assume the upright position it would take very little muscular effort to block up the pelvic outlet and resist the intraabdominal pressure, and even if in childbirth a torn canal resulted there would not follow the dire results which now attend such lesions.

We must then examine the pelvis and its intrinsic parts in the normal *upright position.* This is obtained by holding the pelvis so that the anterior superior spines of the ilium and the symphysis pubis are in the same vertical plane. By careful examination of the living woman standing you will find that this position is correct. Studying the pelvis and its contents in this normal upright position, we are impressed with several important facts:

1. The "white line" forms an angle above the horizon of thirty-three degrees. This angle is open to the rear.

2. The iliococcygeal fibers of the levator ani pass only slightly backward but *mostly downward* into the rectum, ano-coccygeal raphe and the coccyx.

That the pubo-coccygeal (pubo-rectal) portion of the muscle takes a course *almost horizontally backward* around the vagina to its insertion into the perineal center, rectum, ano-coccygeal raphe and coccyx.

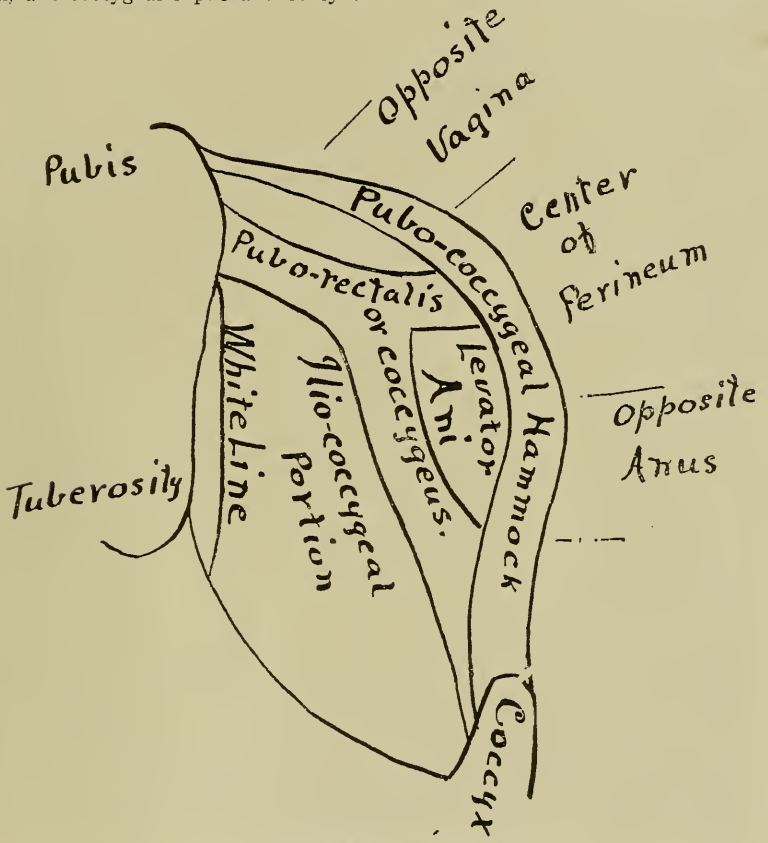

Fig. 9.—Diagram to explain Fig. 8.

The coccygeus muscle can be disregarded in this consideration, as it has no bearing upon the later aspects of the subject. It merely completes the pelvic diaphragm by closing up the gap left between the levator ani, great sacrosciatic ligament, the side of the coccyx and the end of the sacrum.

3. The perineal shelf forms an angle with the horizon of only 3 to 5 degrees. The angle is below the horizon and opens to the rear. The angle is so small that *practically* the *perineal shelf* is in a *horizontal plane.*

4. The course of the vagina from the uterus to the surface is either straight or very slightly curved, the concavity being directed forward or the upper two-thirds maintains this forward curve and the lower third turns slightly backward.

The vagina lies close to the pubic arch, being distant from it (in formaline hardened specimens) seven-eighths of an inch (the urethra intervening). The posterior wall of the vagina is in close contact with the anterior.

5. While the vagina and the rectum are in close contact above the pelvic diaphragm, below this septum they rapidly diverge.

This separation is caused by the abrupt backward turn that the anal canal makes with the rectum. The angle between these two portions of the gut varies from a little less to a little more than 90 degrees. The distance of the apex of this recto-anal angle from the subpubic angle is one and one-fourth inches. The long axis of the anal canal is at an angle of 15 degrees or less with the horizon.

Fig. 10.—Female cadaver which showed a typical laceration of the pelvic outlet. A, B, opposite the posterior pair of caruncles, which are widely separated by the old laceration. This specimen shows the characteristics of a ruptured pelvic outlet. The gaping orifice, the visible cystocele, the shortened perineum, the tip of the rectocele and the relaxed anus are all apparent; C, opposite the clitoris; D points to the external urinary meatus.

6. The space between the anal canal and the vagina is filled in by the perineal body, 1 inch in depth and 1⅝ inches measured along the perineal raphe.

7. The vaginal and anal orifices are inclosed within and supported by the fibers of the pubo-coccygeal hammock, and the center of the vaginal orifice at the hymen is one-fourth of an inch lower than the center of the anus.

What Prevents Prolapse of the Pelvic Viscera?

Examination of the specimens and investigation upon the living show conclusively that the *levator ani muscle* and especially its pubo-coccygeal (pubo-rectal) portion is the *important contractile element present.*

Examination of the living woman with intact pelvic outlet shows the two (anterior and posterior) vaginal walls in close contact with each other; the anterior wall

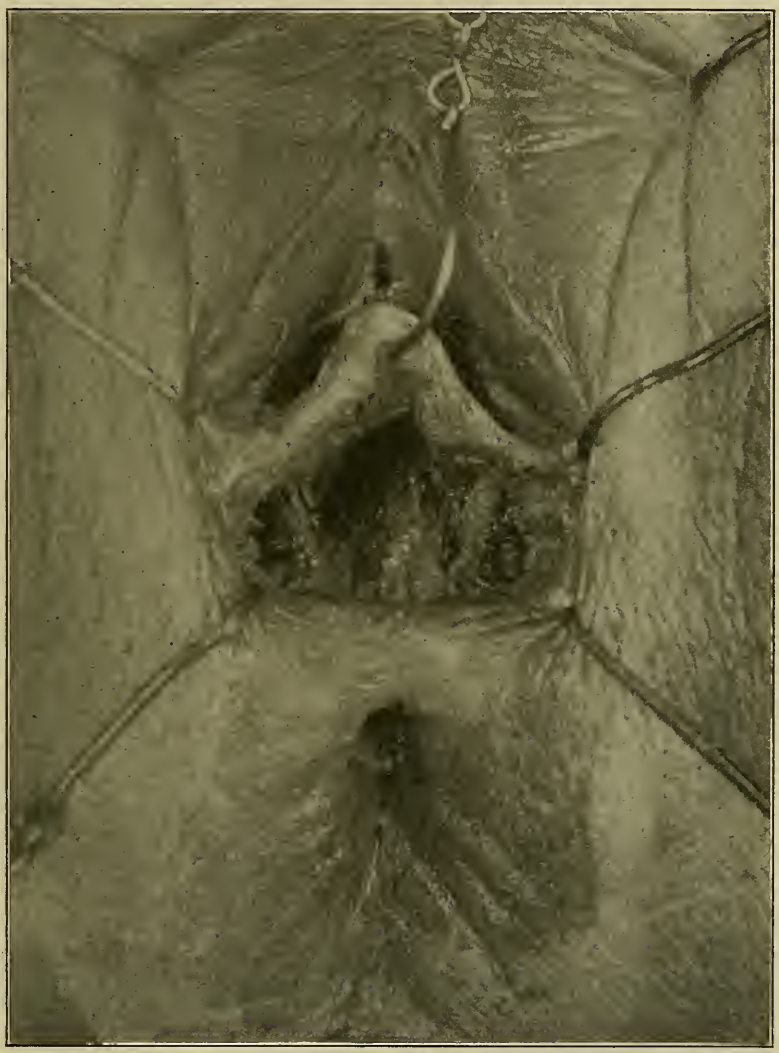

Fig. 11.—Showing the flap-splitting process by which the vaginal and rectal walls are separated and the pubo-coccygeal portions of the levator ani muscle exposed.

is so close to the sub-pubic arch that it really appears to lie immediately against it, except for the urethra intervening between the two along the center.

By pressing strongly backward, the vagina is opened and the two band-like bundles of the pubic portion of the levator muscle will be felt on either side. If now the woman is asked to contract her muscles you will feel the finger drawn up to the pubic arch by the forcible contraction of these bundles as they draw the rectum (recto-

anal angle) and perineum forward. By this mechanism the vagina is firmly closed. At the same time the rectum, at the recto-anal junction is primarily closed laterally by the contraction of these same bundles and drawn bodily forward toward the pubic arch. The lower portions of both canals are maintained in a closed state by the action of the two superficial sphincters.

While the levator ani is the efficient cause for the closure of the pelvic outlet, we must not lose sight of the fact that the upper and lower fascia of the muscle greatly assist in this function.

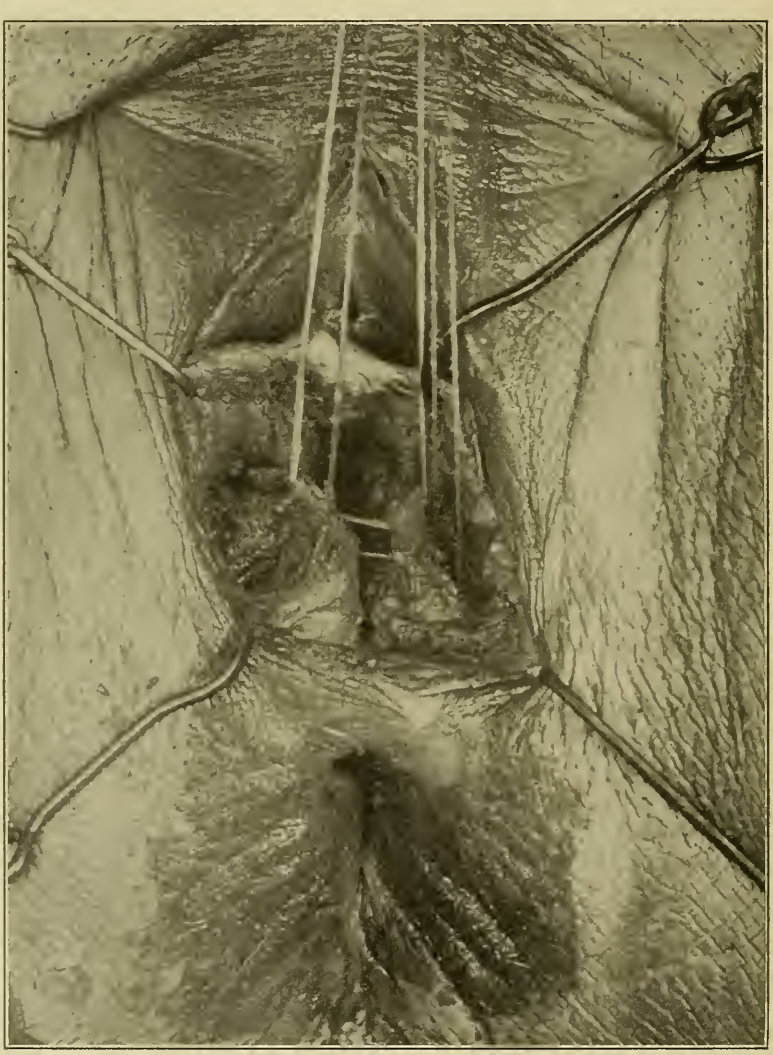

Fig. 12.—Sutures introduced into the pubo-coccygeal portion of the levator ani.

These layers bind the rather loose fibers firmly together, bridge over weak places in the muscle, thus solidifying it and conserving the action of the entire muscle. The strong horizontal perineal shelf at the anterior portion of the outlet plays an active part through its insensitive nature in sustaining the pelvic load without fatigue, and the active muscular arrangement forming the pubo-coccygeal hammock must contribute not a little in assisting the pelvic diaphragm in its function.

III. Lacerations of the Pelvic Outlet.

How Produced—The lesions considered in this paper are produced at childbirth by the passage of the child through the parturient canal, either unassisted or aided by the use of the forceps.

Probably the premature application of the forceps or their faulty adjustment or ignorant use contribute to the production of tears of the pelvic outlet. Indeed, it is probable that the rarer form of rupture of the levator ani muscle close to the pubic

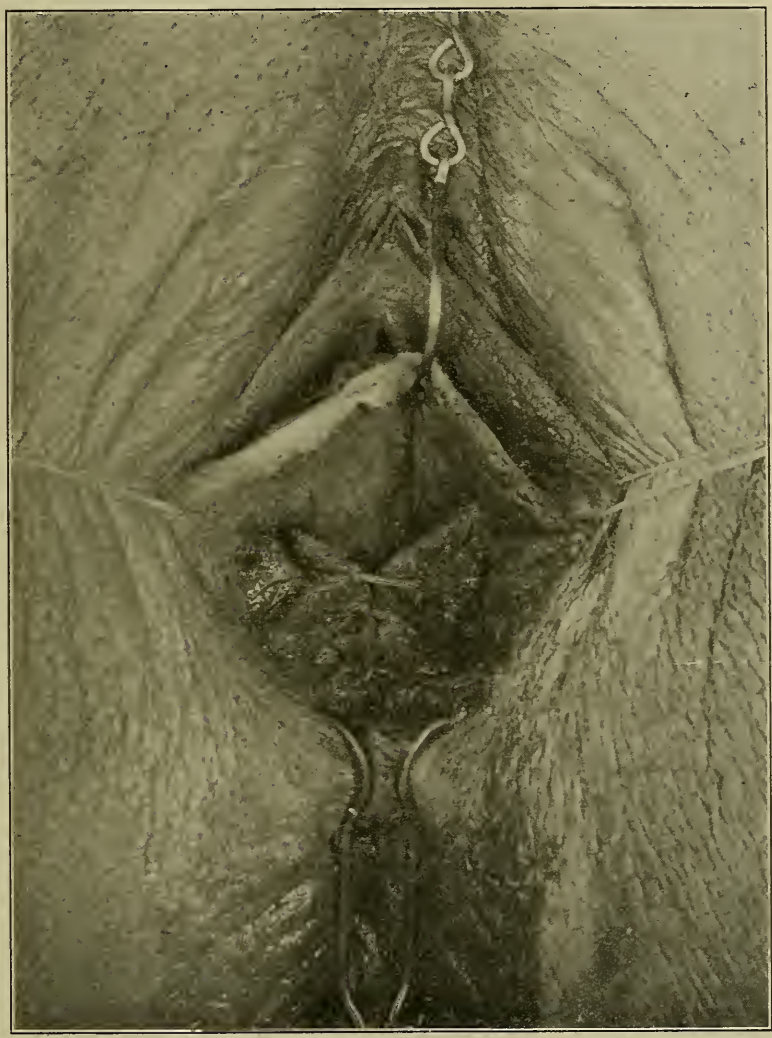

Fig. 13.—The sutures into the pubic portion of the levator ani have been tied. This re-establishes the insertion of the pubo-coccygeus (pubo-rectalis) into the perineal center, and at the same time obliterates the rectocele.

arch is due solely to the cutting action of the blade of the badly applied or used forceps.

At birth, then, the child must pass through the pubo-coccygeal (pubo-rectal) loop of the levator muscle, through the gap in the perineal shelf, and through the vaginal slit in the pubo-coccygeal hammock.

This passage is usually made without any material damage when the normal conditions affecting mother, child and time prevail by the gradual stretching of the structures composing the different layers. However, there may be such a disparity between the size of the child and the potential passageway or the birth so precipitate that all the structures are torn through into the rectum or into the ischio-rectal fossa. Between these two extremes there are all grades of lacerations.

Fig. 14.—The sutures which bring together the ruptured "perineal body" have been placed and tied. The manner in which this builds up the perineum can be easily demonstrated by consulting the preceding photographs. By these sutures the insertion of all the superficial muscles into the perineal center is re-established and the "perineal body" restored to its normal condition.

Extent and Location of the Lacerations:

Lacerations of the more superficial structures, *i. e.*, the perineum itself, independent of the pelvic diaphragm, may occur. When these are shallow they produce no symptoms and need not detain us. If of a more severe character—into the anus, for

instance—they may be dealt with by the operative procedure given in the following pages.

The serious lesions are tears in the pelvic diaphragm, alone or associated with those of the perineum.

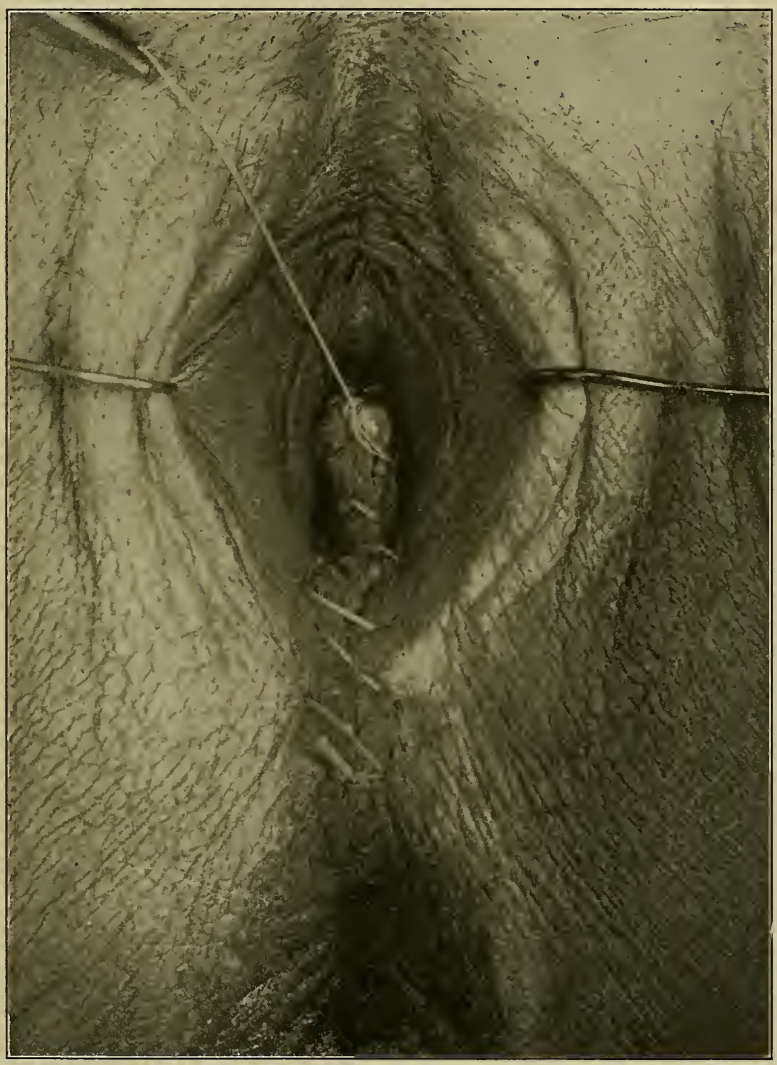

Fig. 15.—Suturing the flap formed of the posterior vaginal wall in a vertical direction. A small gap is left at the posterior end of the incision.

Note that the posterior pair of carunculæ, which are shown in Fig. No. 10, have been brought in contact with each other, thus restoring the outlet to its normal condition. In the living this line of suture should be made with No. 2 ten-day chromic gut and placed in a neater manner than shown here.

These lesions are situated opposite the posterolateral angles of the vagina and are usually bilateral, but the left side usually suffers more than the right. When they are limited to one side only, it is the left which is usually affected.

These lacerations extend for varying distances into the ischiorectal fossæ, severing the pubo-coccygeal (pubo-rectal) bundles of the levator muscle, the transversus perinei

deep and superficial, the triangular ligament and the common attachment of the sphincter ani and sphincter vaginæ.

If the rupture is in the median line the parts are severed toward, up to and even into the anal canal (possibly into the rectum). If the rarer form of laceration is present, the pubic portion of the levator muscle is torn off close to its origin from

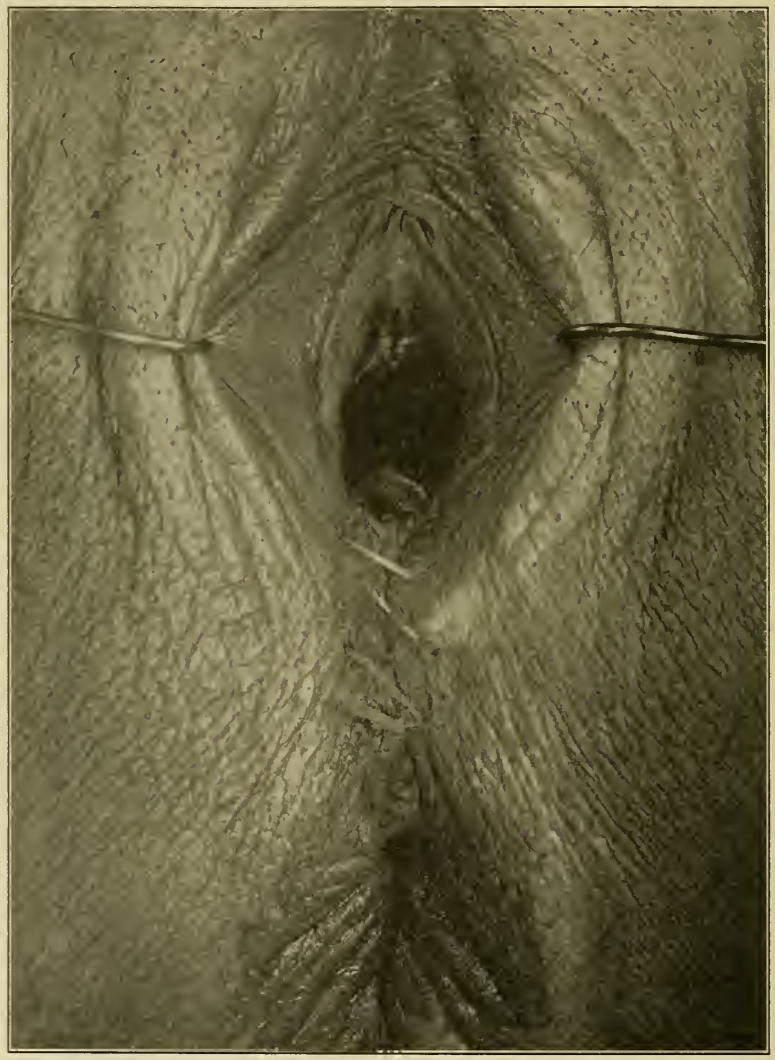

Fig. 16.—Labia widely separated to show how the sutured posterior vaginal wall does not (even in the cadaver) obstruct the vaginal outlet. In the living this excess of tissue will gradually disappear.

Note the depth of the perineal body. Compare with Fig. No. 10 to see how the perineum has been built up between the vagina and the anus.

the public arch. Cervical lacerations, rupture of vessels and damage to the urethra, bladder or other parts are not considered in this connection.

IV. Effects of Pelvic Lacerations.

Superficial median tears produce no symptoms and require no treatment. Lesions of the pubic portion of the levator ani muscle and fasciæ, unless repaired at their in-

ception, will be followed by very serious results as the action of the most important portion of the muscle is lost. The rectum is not drawn firmly against the vagina and both against the subpubic arch. There is, therefore, no support to the anterior wall of the rectum, neither is there any posterior support for the vagina. This loss of sustaining force is felt by the rectum, vagina, bladder and other pelvic viscera. Beginning with the lowest structures and working upward, these viscera gradually fall out of the pelvic cavity through the gap left between the subpubic arch and the ilio-coccygeal loop of the levator muscle. The extent of their fall is limited only by the length to which the ligaments, vessels and nerves which pass to them will stretch in the given period of time.

This fall is aided by the intraabdominal pressure from above. There is thus produced the ordinary retrocele, cystocele, and pouting vagina. Later the uterus and its adnexa and the remaining contents of the pelvic cavity participate in the downward movement.

In speaking of the supporting function of the pelvic floor I have used the term of the "pelvic load" because the weight to be borne is not merely rectum and vagina alone, nor bladder and uterus, but it is in reality the entire column of visceral structures which reach from the pelvic floor to the diaphragm, plus the force exerted by the contracting muscles bounding the abdominal cavity in producing and maintaining the intraabdominal pressure. When the pelvic floor is incompetent to sustain this load there is a displacement of it downward, and the parts to show this displacement or prolapse first are those in closest proximity to the breach in the floor. While Nature has arranged to support these organs by numerous ligaments and vessels with the enveloping connective tissue, and they fully perform this function while the pelvic floor is intact, and while they can support the load for a time even if the pelvic floor is damaged, yet, after a variable time in this last condition, these ligaments gradually stretch, the viscera drop downward and a condition of prolapse of the organs becomes evident. The superimposed abdominal viscera also share in this downward movement.

Diagnosis of Pelvic Lacerations—Inspection shows a pouting, swollen, open vaginal orifice, through which may be seen the tip of a rectocele and a cystocele. The anus is relaxed and prominent.

The interval between the vaginal and anal orifices may be greatly reduced and even destroyed.

A cicatrix fills the interval between the posterior extremities of the labia. The anterior limits of this cicatrix is usually indicated by the most posterior pair of caruncules. (These caruncules also indicate the points between which the mucocutaneous incision extends.)

Digital examination confirms the general thickening, swollen and lax state of the parts. The cervix will usually be encountered close to the vaginal orifice. Pressure backward encounters no resisting pubo-coccygeal bundles of the levator ani, and, upon voluntary effort by the patient, there is no muscular action of these fibers to compress the vagina, and to draw the rectum (recto-anal angle) forward toward the subpubic arch. There is only a weak lifting of the anal portion of the perineum, due to the action of the ilio-coccygeal portion of the muscle. A finger in the rectum finds the anterior wall of the recto-anal angle ballooned out and projecting downward and forward into the vagina as the rectocele. A sound in the bladder shows that there is a similar pouching downward and backward of its base so as to produce the cystocele.

The uterus and adnexa in the early stage of the process may show no disturbance in position, but later they all share in the downward movement and this may go on until the uterus projects through the vaginal orifice, and the adnexa are prolapsed into the funnel-shaped pouch of Douglas. Between these extremes there are all degrees of displacement. Prolapse of the intestines will be sure to keep pace with the fall of the pelvic viscera, and all sorts of abdominal ptosis may be associated with a ruptured pelvic outlet.

Repair of Pelvic Lacerations.

This paper is confined to the treatment of pelvic lacerations, even though such lesions are followed by all the pathological conditions mentioned above, as cystocele, rectocele, uterine displacements and numerous other pelvic conditions. I do not intend to rehearse all the measures which should be instituted for the relief of such conditions as it would unduly lengthen this paper and confuse the real point I wish to emphasize, viz., the proper repair of the ruptured pelvic floor.

Besides the operation advocated for this lesion, the other pathological states demand surgical treatment, and, although these measures will not be outlined here, it is understood that they should be done.

The mechanical features of rectocele, cystocele, displacements of the uterus, tubes

and ovaries; the functional ones of constipation, disturbed micturition, abnormal menstruation, congestion and inflammation of the pelvic viscera; and the mental ones of growing discomfort to actual distress in the pelvic region and reflected areas, bring the woman with a lacerated pelvic outlet to the operating table.

Until Emmet made the distinction clear between lacerations of the levator muscle and the "perineal body," the operations proposed for the relief and cure of these conditions had no anatomical or logical foundation. Emmet demonstrated that there could be an extensive tear of the "perineal body" without any other symptoms objective or subjective, and, that there were cases with intact perinei in which existed prolapse of all the pelvic organs.

The essential distinction is as has been pointed out that in the latter case the levator muscle has been torn while in the former it remains uninjured.

The lesion then is situated in the pubo-coccygeal (rectal) portion of the levator ani muscle. It is usually at the postero-lateral angle of the vagina, and it may be unilateral but is usually bilateral. Median tears may also exist. The treatment of these conditions is the same. The problem is how to expose the parts and repair the damage.

There have been any number of operations proposed, but they all may be grouped under two classes, denudation and flap-splitting. While I have performed both operations many times, the denudation method first and later the flap-splitting operation, I must say that to my mind, the latter plan is the only one which, when carried out to the extent here advocated, will fulfill all the indications demanded.

It is founded on true anatomical and surgical principles, and the results prove its correctness.

By the flap operation no tissue is lost, the exact site of the lesion is exposed, viz.: the levator ani and its enveloping fasciæ, the sphincter ani and the transversus perinei. The operation is easy of execution and rapidly performed. All sutures are buried and do not require removal.

The Operation—The incision is made with scissors along the mucocutaneous border of the vaginal orifice, from the anterior margin of the cicatrix on one side to a similar point on the other side. This forms a "U-shaped" incision.

With the scissors and fingers the vagina and the rectum are quickly separated from each other, from the perineum to the highest point of the rectocele, and laterally so far outward as to sever all the cicatricial bands and fully expose the margins of the levator ani muscle. Two or three chromic gut or kangaroo sutures are placed in the margins of the levator ani, taking care to pass the needle outward, deeply enough to get a firm hold of the muscle and its fasciæ. The number of sutures depend upon the width of the gap to be corrected, and no fixed number can be given; place enough to obliterate the rectocele and properly close the gaping vagina.

Control hemorrhage, which will be quite free, but as it is mostly venous pressure and hot sponges are usually sufficient, and tying the sutures in the muscle will arrest what remains. Next place one, two, or three sutures of the same material in the lateral surfaces of the wound superficial to the levator muscle. These sutures are placed deeply and they must necessarily without further dissection, gather up the sides of the severed perineal body and bring once more into a central insertion the sphincter ani externus, sphincter vaginæ and the transversus perinei muscles, and, furthermore, they will also reunite the deeper parts of the perineal shelf.

The operation is finished by suturing the "U-shaped" incision vertically with No. 1 or 2 ten-day chromic gut. There is a small gap purposely left at the posterior angle of the incision for drainage, as there will be some oozing for the first twenty-four hours. The redundant flap of vaginal tissues is tucked into the vagina and the operation completed.

This operation gives perfect and complete exposure of the damaged structures at the site of the lesion. The reformation of the central attachments of the various structures of the pelvic diaphragm, perineal shelf and pubo-coccygeal hammock cures the rectocele, restores the vital action of the pubo-coccygeal bundle, brings the posterior wall of the vagina forward against the anterior, narrows the vaginal canal to its proper size, reforms the pelvic floor, furnishes a firm support for the intraabdominal pressure and a solid basis for any further work upon displaced pelvic viscera.

If such a repaired outlet is carefully examined two or three months or years after the operation you will notice these points of improvement. The vaginal orifice is not gaping but closed. There is the normal space between the vaginal and anal orifices, and the perineum has its normal contour. A finger in the vagina shows its two walls in contact, and if the muscle is called into action the finger will be carried against the subpubic arch by the forward movement of the rectum (recto-anal angle). Furthermore, the perfection of the result is asserted by the patient and proved by subsequent childbirths.

INJURY BY ELECTRICITY.*

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In view of the widespread and increasing industrial use of electricity it is not surprising that electric trauma is on the increase and that cases thereof are being cited in medical publications. Despite this, authoritative information as to the physical effects of electricity is very scanty (1), especially in American literature. In Germany (notably through the investigation of Jellinek) (2), and in France and Great Britain, there has been much preliminary experimentation and subsequent case reporting by physicians; but in this country investigation has been limited almost solely to electric engineers, and case reports have been few in number. This is my excuse for bringing the subject before the section as this paper aims to narrate what has been learned from personal observation and a very considerable search of the available literature.

TECHNICAL TERMS.

For an intelligent understanding of the matter, it is necessary to know some of the usual technical terms, and they can be stated thus:

The *volt* is the unit of pressure. The *ampere* is the unit of strength. The *ohm* is the unit of resistance. The *coulomb* is the unit of quantity.

But for all practical medical purposes it is enough to remember that volt is the unit to express pressure, intensity or electromotive power; and that the ampere denotes strength or current quality. The volt is the impelling force which moves the electricity through any conductor. The ohm is the unit of resistance and expresses that quality of the conductor which resists the passage of electricity through it.

Electricity flowing through any conductor is impelled by the voltage of the circuit and is opposed by the resistance of the conductor. The size of the current which flows is directly proportional to the voltage and inversely proportional to the resistance. This "size" is measured in amperes, the ampere being the unit of current, and its numerical value is found by dividing the volts by the ohms; (A=V/O; "Ohm's Law"). Ordinary conductors carry currents of three varieties; direct (or continuous); alternating; and interrupted.

The contact may be of four kinds, viz., *positive,* where the body is firmly and constantly pressed against the conductor; *partial,* where the contact is slight and steady; *brushing,* where the contact is slight and for a short interval, and *arcing* where the current reaches the body via a vapor through which the current passes. The *intensity* may be (1) *low* (100 to 300 volts); (2) *medium* (400 to 600 volts); *high* (1,000 volts and over); this classification being that adopted by Prevost and Batelli, of Geneva, as the outcome of many experiments.

The *duration of contact* may be (1) *short,* from one to five seconds; (2) *medium,* from five to eight seconds; and (3) *long,* from eight seconds upward.

Mode of receipt is generally by charged (1) wires or rails; (2) metal apparatus or tools; (3) flashes or arcs which are productive of burns only.

The average electric pressure in electric lighting is from 100 to 225 volts (direct), usually about 110 volts; in overhead and underground trolley systems from 500 to 600 volts (direct); suburban lighting circuits 1,000 to 2,000 volts (alternating); series arc lighting circuits 2,000 to 4,000 (direct or alternating); in overhead, long haul railway systems (as the N. Y., N. H. & H. R. R. Co.) 11,000 volts (alternating). In the third rail systems, like the local subway, the voltage is about 550 (direct). The highest voltage transmitted by wire in this country is that generated from Grand Rapids, Mich., 100,000 volts. Another system in Denver transmits 88,000 volts, and one in Los Angeles 75,000, and that from Niagara Falls 60,000.

A voltage of from 200 to 500 is usually not dangerous, but the alternating current is considered to be more dangerous than the direct. In the electrocution of criminals from 1,300 to 2,000 volts are used, the average being 1,700 of the alternating type.

* Read before the Surgical Section of the New York Academy of Medicine, March, 1909. Reprinted from the Journal of the American Medical Association, April 2, 1910.

Factors Influencing Physical Effects.

The physical effects are mainly determined by the following:

1. Amount and duration of current.
2. Site, type and area of contact.
3. The individual.

Amount and duration of current is the main essential, and the greater the degree and the longer the duration, the greater the effect. High voltage, long duration and positive contact generally predicates coma, severe systemic shock, burns and oftentimes death. Medium intensity, with medium duration and partial contact, generally means burns of the second or lesser degree, less profound coma and shock with more or less paresthesia, especially numbness and tingling. Low intensity, with short duration and brushing contact generally means burns of the first degree or none, slight, if any, coma, and moderate paresthesia mainly of the tingling type. Low intensity, with brief duration and partial contact, generally means absence of burns or systemic symptoms, paresthesia of the formication type being generally alone complained of.

Amperage is so variable that it has not been mentioned because of its uncertainty, but the higher it is, the greater the effect in general.

Site, type and area of contact is less important, pursuant to the physical law that electricity takes the shortest route between two electrodes, and this has led to investigation to determine the resistance of various bodily elements to the transmission of electrical energy. It has been found that the tissues transmit proportionate to the amount of their fluid constituents; the more saline this is, the better the conductivity. Blood is the best conductor, mainly because of the saline serum. Muscle comes next, nerve tissue follows, and bone is a poor conductor. Similarly, experiments have shown that the bodily tissues exert varying resistance to the passage of electricity, as denoted by the unit of resistance, the ohm. The average human resistance is 1,000 ohms. Dry skin is very resistant, and one observer (Jolly) says that this is 150 times greater than that of the underlying tissues. A dry, hard, thick skin offers more resistance than one that is moist, soft or thin; an acid or alkaline perspiration reduces the resistance, while an oily skin raises the resisting power. If a strong alkali be applied to the skin so that the oily secretions are removed, the resistance is much lowered, so that the subject experiencing little effect from 100 volts might be disturbed by 10 volts. Larrat (3) says that if muscle is given a standard resistance of 1, then nerve and cartilage can be denoted by 2.5; bone as 15 to 20; and the skin and epidermis as between 100 and 500. Electric energy meets greater resistance passing transversely to the axis of a tissue than when transmitted longitudinally, this being 6:1 in muscle, 3:1 in nerve fibers. Turner's experiments indicate that transmission from hand to hand meets with a resistance of 1,375 ohms; through one hand 900 ohms; from cheek to cheek 600 ohms; from one supramalleolar region to another 700 ohms; and through the calf of leg 350 ohms.

As compared with any metal, the body is a poor conductor, it being calculated that muscle is 115 million times a poorer conductor than copper. It has also been estimated that one inch of the sciatic nerve has eight times the resistance of the Atlantic cable. (4)

The greater the area of contact, the greater the effect, especially if the current traverses vital parts, notably if the heart is in circuit.

The individual variation means the personal equation, and it is strikingly similar to that of drug idiosyncrasy, notably as to sex, age, physique, occupation and temperament. Males are less affected than females; the aged offer less resistance than the young on account of the constituents of the blood vessels; those of rugged and muscular physique have a greater conductivity than those of the opposite type; the phlegmatic are subjectively less prone than the neurotic; those accustomed to electric energy are often less influenced than the novice. Illness, sleep and alcoholism render persons less sensitive. (5)

Variations as to the time of day, type of clothing, amount of food in the stomach and general well being, all seem to exert some influence; but the given effect cannot always be determined by these factors, and I have known electric workers to have practically no effects from contact under circumstances that left no doubt as to high voltage traversing the system.

Physical Effects.

In a general way these are three in number:

1. Death.
2. Burns.
3. Nervous symptoms.

Death.—Death from electricity is usually sudden, and is best represented by the execution of criminals, lightning stroke and unexpected contact with highly charged materials, the body completing and short-circuiting two conductors. Under such circumstances there may or may not be decided external evidence of what has occurred, any such taking the form of burns of varying degree, areas of lividity or ecchymosis, or simple crimsoning to mark the place of entrance or exit of the current. It is, however, very unusual for a lethal dose of electricity to fail to leave some visible evidence at the points of contact. Postmortem, such cases are surprisingly free from gross microscopic changes, and the most careful search of all the tissues has as yet failed to give any adequately uniform cause of death. The findings in general are not unlike those following drowning or suffocation. The body of Czolgos, assassin of President McKinley, was subjected to the most minute scrutiny, especially by Spitka's examination of the brain and cord, but nothing more than the customary fluidity and venous stasis of the blood with flaccidity of the heart muscle was found. In a still more recent autopsy of an electrocuted murderer the same negative findings were recorded. Observers appear to have two main theories to account for death under such circumstances; one being that the heart muscle is paralyzed by a tetanic spasm analogous to that observable in skeletal muscle under high voltage; and the other theory, that there is a definite cellular destruction, especially of the vital centers. In connection with this last, it has occurred to me that the disintegration that seemingly takes place may generate toxic materials, thus adding a chemical to a mechanical irritation that almost immediately kills. Death from low tension current is by heart fibrillation; heart and respiration alike fail from lethal medium tensions; and respiratory failure is the cause of death in high tension accidents (6).

Burns—Burns by electricity differ from those due to extremes of temperature only in origin, and they may be of the usual first, second and third degrees. An electric burn is an index of resistance of the tissue affected, and always indicates that the full strength of current has not been received. The character of the burn is sometimes determined by the type of metal acting as a conductor, and burns by arcs and flashes from copper conductors sometimes produce less severe burns than those emanating from iron or steel. By contrast with burns, due to flame, or contact with steam, hot solids or liquids, deep electric burns are apparently less painful, produce less systemic shock, and heal more quickly. This was vividly impressed on me in a recent Harlem hospital service, where in adjacent beds lay patients who sustained irregularly distributed burns of all degrees in an incendiary fire, and also those who had received "third rail" burns; the former had more systemic symptoms, the burns were more intractable to treatment, and the complaints of pain were greater than in the latter class of cases. This is probably due to the fact that electric destruction of tissue is sudden and absolute, as if done by electric cautery. The contrast is even greater by comparison with burns from hot liquids, such as boiling water, oil or tar, and this irrespective of the surface areas involved. The resultant scarring and contraction appear about equal, even though electric burns are often more diffusely distributed over widely separated areas than burns of other kinds. If the clothing is ignited, there is added the element of heat burns to those which may be the direct result of electric contact. Examples of "third rail" burns are shown in the annexed illustrations (Figs. 1 and 2).

Burns resulting from partial or arcing contact often heal slowly and show a tendency to slough or to become gangrenous, especially if the trophic supply be involved. Cases of this type sometimes give external signs disproportionate to the underlying damage, and the severer symptoms may be a few days in appearing, and then show an isolated or confluent areas of a more or less gangrenous type. From the time of receipt of burns of this kind to the outbreak of severer manifestations, the interval period is always filled by symptoms indicative of more or less deep seated damage, in addition to the superficial evidences.

Report of Cases.

As chief surgeon of the Metropolitan and Interborough Railways I have had many opportunities to examine cases of electric injuries, and one of the worst of these was the following:

Case 1—*History*—S., a laborer, was working in a manhole repairing the "channel rail" of one of the surface roads, the current of 550 volts being turned on. In some manner he fell against this charged rail so that his back contacted at about the lower scapular level, his feet being grounded on concrete.

Examination—He remained in that position several minutes, and when released

was found to have a third degree burn that practically escharred his back from mid-scapular to the lower lumbar region, and it is said that the burn reached far enough to expose the underlying viscera. He suffered profoundly from shock and was unconscious, and his recovery was protracted. Even at this date (6 years later) there is an unhealed area about 3 or 4 inches in the central portion of the scar, but all except this space cicatrized without skin grafting in a remarkable way considering the original extent and severity of the wound.

Subsequent History—Some years later he was seen and exhibited by me, and at that time he had a butterfly-shaped scar 13½ by 11 inches in the involved area, in the lower portion of which was a supposed lumbar hernia. The scar had contracted enough at first to almost draw the wings of his scapulæ together and spinal flexion was impossible; but by continued self-bending and manipulation of his back, he so far recovered as to be able to resume manual labor. Later he was operated on by me and the supposed lumbar hernia proved to be retracted bundles of muscle fiber. The above mentioned unhealed areas were covered by autogenous Thiersch grafts, but healing was not yet complete in January, 1910. He at no time developed a traumatic neurosis (Fig. 3).

Fig. 1.—Example of third-rail burn.

Case 2—*History*—Another severe case was that of D. H., aged 23, ironworker, born in Finland. He was working on an iron trestle repairing overhead wires of a suburban electric and steam railroad, and, while assuming an upright position, his left occipital and clavicular regions contacted with a wire bearing 11,000 volts, and he became temporarily unconscious. Through the courtesy of Dr. F. B. Littlewood he was seen with this physician ten days later at the New Rochelle Hospital, and at that time he was able to be out of bed for a portion of each day.

Examination—He then presented numerous sloughing and granulating burns of the left upper extremity and chest, and an extensive third degree burn of the left occiput and of the soles of the feet. He had little if any systemic shock or sepsis. There was no nervous involvement organically or functionally. Mentally he was as apt as could be expected, considering the fact that about one-sixth of his body was more or less badly burned.

The duration of contact in this case could not be ascertained, but it must have been short and imperfect, as it is to be noted that the contact was on the head and the left upper extremity, and that he was grounded by his feet standing on a metal

support so that the main part of his body was temporarily a part of the circuit. He wore no hat, and his shoulders were bared except for a thin shirt, and he had no tools in his hands. Theoretically this man should have been unable to withstand electric shock of that volume, but the burns evidenced the fact that only a portion of the voltage was received. I am told by Dr. Littlewood that he made an excellent recovery, and that his progress and subsequent symptoms were those typical of severe burns.

Case 3—*History*—I am also indebted to Dr. Littlewood for notes of the case of J. M., who was working on the same railroad and who came in contact with a transformer so that his left shoulder apparently received 11,000 volts.

Examination—He immediately became unconscious, and when seen at the New Rochelle Hospital by Dr. Littlewood, had severe burns of the entire left half of the body, and the sole of each foot showed two large blebs about the circumference of a dollar. His temperature ranged from 98 to 99.4, pulse 99 to 120, respirations 20 to 40. The next night he began to vomit, and developed an uncontrollable singultus. The vomits became biliary, and assumed the type seen in gastroduodenitis following severe burns of this or other origin.

Fig. 2.—Example of third-rail burn.

He died early on the fourth day apparently from systemic shock. In this case the manner and duration of contact was problematical, but it is stated that the contact was for an appreciable time and that he was probably grounded on metal judging from the blebs of the feet. It is to be noted that the respiratory rhythm was more disturbed than that of the heart, and that his temperature was at no time more than one-half degree below normal. Death in this instance was probably due to respiratory failure accompanied by paralysis of the diaphragm. No autopsy was permitted. The cause of the gastroduodenal symptoms in any class of severe burns has never been satisfactorily explained, and it is generally a bad feature.

Nervous Symptoms.

In the absence of direct destructive or inflammatory damage to nerve fiber and the subsequent development of a more or less localized neuritis, the nervous effects are almost invariably those of the hystero-neurasthenic type, it being rare in my experience to find either neurosis separately as a consequence of electric or any other form of trauma. I have never known an organic disease of the central nervous

system to develop from the passage of electricity through the body, nor does the available literature narrate more than one instance of this nature. If a direct injury has been done to nerve fiber, the symptoms will be those corresponding to the distribution of the affected nerves, and hence no description is needed.

Where direct injury to nerve tissue is absent or minor in extent, the subsequent development of neurasthenic and hysterical symptoms is generally psychic in origin or dependent on auto- or hetero-suggestion, and the signs then presented are usually disproportionate to the actual physical damage sustained. Such cases rarely present objective evidences of electric contact and occur usually in those predisposed because of a neurotic or actually hysterical temperament. The flash or spark or arc from charged metallic contacted points occasionally induces this set of nervous symptoms, either with or without bodily contact. Cases of this and allied sorts are often designated by the term "electric shock," and less frequently as "electric neurosis;" but the symptoms do not differ in any essential respect from the ordinary shock or neurosis attributed to any other trauma.

Fig. 3.—Third degree electric burn extending from mid-scapular to lower lumbar region.

Examination of such a patient develops a wealth of subjective symptoms and a poverty of objective symptoms, and the average case will correspond to the following:

Case 4—*History*—Mrs. F. was alighting, during a rain, from a suburban electric car operated by the overhead trolley system. While she had one foot on the car platform and the other on the metal step, her hand being on the dash handle, she claims to have received a "shock," the force of which threw her face downward to the ground. She was stunned but not unconscious, did not vomit, and when assisted to the adjacent sidewalk was able to discuss the occurrence with some show of agitation and not a little anger. She walked unaided to her home near by and saw her doctor some few hours later. He gave her lotions for the bruises of the knee, elbow and hands. There were no burns or obvious electric effects, but she did complain of tingling and needle sensations in the hand that touched the dash-handle and in the foot that contacted with the metal step.

Examination—When I saw her some fourteen days after the accident she was abed, somewhat pallid, and had a characteristically tense and drawn expression, and was markedly irritable in manner and speech, all of the foregoing being said to be foreign to her normal state. There was an obvious rapid tremor of the closed eyelids, about the angles of the mouth, and of the outstretched fingers and protruded tongue. External evidences of injury were lacking aside from a fading area of bluish discoloration over a palm-sized area just above the right knee, probably from her fall. No evidences of electric contact, or of so-called "electric shock" were apparent. No paralyses and no areas of diminished sensation; conjunctival and pharyngeal reflexes absent; marked dermographia; knee-jerks lively, all others normal. Romberg sign marked; no Babinski, or allied manifestations. Gait was normal and pulse rapid. There were areas of shifting tenderness along the spine, these being very inconstant and readily brought out by suggestion. Two spots were found in the upper dorsal region consistently tender, but she leaned back in a chair on these same areas and made no complaint. There was no contraction of visual fields, and no color distortion. Here is a typical case of the milder form of recoverable hystero-neurasthenia, and she had many symptoms that might as well be stigmatic as symptomatic. She recovered perfectly in a short time.

Contrasted with the former mixed type of functional nervous disturbance, the following case of almost typical hysterical motor paralysis with milder neurasthenic symptoms is narrated:

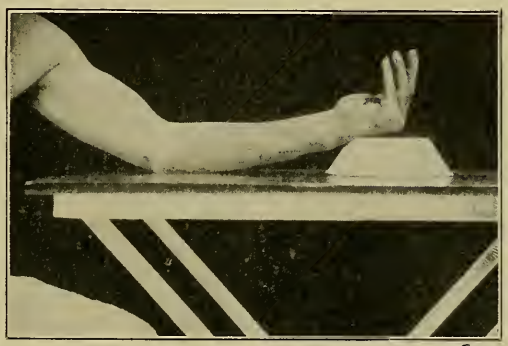

Fig. 4.—Pseudo-Dupuytren's contraction as the result of electric burn, showing marked palmar flexion at the metacarpo-phalangeal joints of the inner four fingers.

Case 5—*History*—G., an electrician, was admitted to the Harlem Hospital in Dr. H. A. Haubold's service with a history of having been injured two weeks ago in an out-of-town power house, the patient stating that while holding a dead wire in his left hand, someone turned on the current of 110 volts and his hands and fingers were burned; immediately fingers of the left hand contracted; it felt as if an electric current passed through him every time his fingers were touched; he claims to have lost all sensation over entire left upper extremity; and says that he cannot move his fingers; he has had other electric burns, but was never affected in this manner before; the current entered the palm of the left hand, but the place of exit is unknown.

Examination—On examination the left hand presented the pseudo-Dupuytren's contraction appearance indicated in the annexed photograph (Fig. 4), palmar flexion at the metacarpophalangeal joints of the inner four fingers being marked, that of the ring and little finger being most prominent. There was no apparent atrophy, nor was there any burn or other sign of trauma. He would not permit the slightest manipulation of the extremity except when his attention was diverted, and then the fingers could be partly extended. He claimed loss of thermal and tactile sensation over variable areas from the elbow down; but these shifted, especially on suggestion, and followed indefinite nerve distribution. Active motion of the wrist was limited; that of the elbow and shoulder normal. He would not permit passive motion, nor would he consent to electric tests. The examination as to his general state showed him to be in excellent condition except that he was of neurotic type and presented many hysterical stigmata and neurasthenic manifestations.

During the fortnight intervening between the accident and his entry to the hospital, he was under the care of a physician, who had given him some internal medication with local application of iodin, and who is said to have made a diagnosis of "paralysis from electric shock." At no time were splints or retentive forms of apparatus employed. He would not consent to the proposed anesthetization, nor would he allow a dorsal splint to be applied, and accordingly he was dismissed from the hospital with a diagnosis of "hysterical paralysis of hand." There was unquestionably an element of voluntary exaggeration in this instance as so often happens in that class of case in which litigation is pending. When seen a month later he had regained function enough to do his usual work but still had many subjective complaints.

Occasionally there are recorded cases in which blindness and deafness and other special sense defects have been attributed to electric contact or flashes, but all instances of this sort are of the hysterical variety, and fall into the class of so-called "fright neuroses." An example of this sort came to my notice recently in which "blindness" was said to have been induced in a susceptible woman by the flash and spark display when an overhead trolley wire was struck by a metal beam. She was seated in her room some two hundred feet away from the scene of this brilliant display of light and sparks but within sight and sound of the occurrence, and she claimed that she experienced the sensation of a ball of fire dancing before her eyes, and she immediately became sightless. Examination showed no organic defect of vision; the case was one of hysterical amaurosis induced by fright in a susceptible person. Vision returned within a short time.

Other Effects.

Crile (7) says that high tension currents produce no chemical change of importance in the various tissues and organs aside from the burning at the place of contact, and that the blood is unaltered. To prove this, a current of 2,300 volts (alternating) was passed through the head of an animal, and during the ensuing month of observation there was no discoverable loss of function. The same observer also says that when atropin is administered before the current is applied, the inhibitory effect is almost wholly obviated, except when the current passes through the heart muscle and then death ensues.

Treatment.

Treatment presents no special problems, inasmuch as it is for the relief of shock, burns or neuroses. In cases of profound injury, and even where death has apparently occurred, prolonged artificial respiration should be maintained, as in drowning cases, with compression of the chest-wall in the precordial region; even digital compression of the heart itself has been proposed, but never successfully practiced. Crile recommends rhythmic pressure over the heart area, the tongue being drawn out, as he says that this combines circulatory and respiratory artificial stimulation.

With the foregoing manual methods, the use of various stimulants of the atropin, strychnin and adrenalin sort is also advisable.

Burns are treated in accordance with the custom of the individual physician, and it has been observed that the so-called open method of treatment is especially efficacious in this type of burn.

Neuroses are best treated by isolation, plus the mental or therapeutic means best liked by the individual practitioner.

Prognosis.

Prognosis depends on the extent of initial inhibition symptoms: in patients that survive forty-eight hours, the prognosis is that of the absorption of septic and toxic products from the burned areas, with the development of cardiac, respiratory or kidney complications, and with, occasionally, the presence of fatal gastro-intestinal disturbances.

The ultimate scarring and contraction from the burns requires no comment. Neuroses do not ordinarily develop until after the patient has recovered from the main objective symptoms, and these nervous manifestations then frequently stand in relationship to a pending claim, and recovery does not usually ensue until adjustment is effected.

Conclusions.

It can be stated that there is no special form of physical effect inherent to electricity inasmuch as every symptom can be paralleled by other forms of trauma. Likewise there is nothing pathognomonic in electric shock and the symptoms of it are those common to other forms of systemic shock, with or without burns or neuroses.

The duration of symptoms is no more prolonged after electric than other forms of trauma; nor does there appear to be any sound basis for the claim that one electric shock renders the recipient more prone to similar experiences, but on the contrary an acquired immunity seems to be created by repeated applications. Electricity is well understood scientifically and is governed by well-known physical laws, and there is no good reason for the view often expressed that its effects on the human economy are unusual or peculiar.

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PERITHELIOMA OF THE CAROTID GLAND.*

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The comparatively small number of cases of perithelioma of the carotid gland, reported in medical literature, would appear to be sufficient justification for the report of the following case:

A. E., female, age 23, domestic, born in the United States, referred to the writer by Dr. J. A. Heitlinger, noticed a small mass about the size of a marble in the left side of the neck several months ago. The tumor was painful and seemed to increase slowly in size, but at times appeared to be larger than at others. There were no subjective symptoms, except that one week before examination the patient complained of hoarseness, which she attributed to a "cold." Unfortunately no laryngoscopic examination was made at this time. The previous and family history was negative.

Physical examination showed an oval tumor 3½ by 2½ by 1½ cm. in the left side of the neck, at the anterior border of the sternomastoid muscle on a level with the superior margin of the thyroid cartilage. The mass was firm in consistency, the surface was smooth, it was freely movable laterally but not in a vertical direction. The skin was freely movable over the tumor. It was not tender and a slight transmitted pulsation was present. No enlarged lymphatic glands were felt. A diagnosis of tuberculous cervical lymphatic gland was made and the patient was referred to Bellevue Hospital for operation.

Operation—In incision about 6 cm. in length, parallel with the creases of the skin of the neck, was made over the tumor, which was found to be situated in the bifurcation of the common carotid artery. The posterior portion of the tumor lay between the external and internal carotid arteries, which deeply grooved its surface. Its capsule, which was exceedingly vascular, was quite adherent to the sheaths of these vessels. It was possible to remove the tumor without injury to these vessels or apparent injury to any nerves. However, the patient's hoarseness was more marked after the operation, and laryngoscopic examination showed paralysis of the left vocal cord, and marked congestion of the mucous membrane of the larynx, especially about the arytenoid cartilages. A recent laryngoscopic examination, for which I am indebted to Dr. Cornelius Coakley, shows that the left vocal cord is still paralyzed but that the thickening in the larynx has almost disappeared, which would account for the improvement in the patient's voice.† It is difficult to account for this par-

* Reprinted from the Medical Record, March 6, 1909.

† When seen recently the aphonia had entirely disappeared, and the patient's voice was perfectly normal.

alysis as the recurrent laryngeal nerve was a considerable distance from the field of operation; the hoarseness was present before the operation, and the increased post-operative aphonia may have been due to the congestion and thickening of the laryngeal mucous membrane, resulting from traumatism at the time of operation.

Pathological examination of the tumor made by Dr. Chas. Norris, pathologist to Bellevue Hospital, proved the growth to be a perithelioma of the carotid gland.

The most recent complete review of the literature on the subject is that of Keen (1) and Funcke, published in 1906, in which they report one case and review the literature of twenty-six additional cases. For the report of these cases, as well as an admirable account of the etiology symptoms and pathology of perithelioma of the carotid gland, the reader is referred to this paper.

Keen collected twenty-seven operative cases including his own, one case in which no operation was performed and two cases reported from post-mortems. In the twenty-seven cases there were seven deaths, a mortality of 27 per cent., due principally to pneumonia from cutting the vagus, or to brain disturbance as a result of ligation of the carotids. In addition to the deaths as an immediate result of operation, one patient died a year after the removal of the tumor from recurrence, and there were three cases in prospect of death from recurrence which had already occurred at the time of Keen's report. One additional case reported but not operated upon was fatal as a result of malignancy. In 18 cases all three carotids were ligated, the external carotid alone in 2 and the jugular vein in 13. The pneumogastric nerve was injured in 6 cases, the sympathetic in 2, the lingual in 2, and the hypoglossal in 4. In addition, Da Costa (2), in an analysis of fifteen cases, included in Keen's list, calls attention to injury of the facial and recurrent laryngeal nerves in two cases of postoperative paralysis of the vocal cord, and reports that the superior laryngeal nerve was injured in his own case.

Since the publication of the article by Keen and Funcke the writer has found the report of but three cases, which, together with one unreported case operated upon by Dr. Wm. Downes, and his own case, make a total of thirty-two operative cases. A brief résumé of the reports of these cases follows, they being numbered as they have been reported after Keen's twenty-seven cases, so as to bring the literature on the subject up to date.

Case 28—Cook (3.) Man, 29 years old, colored. Tumor in left side of neck sixteen years. Operated on nine months previously, but tumor had recurred and at time of second operation was 7 x 5 x 5 cm. in diameter. Diagnosis of aneurysm of the carotid made. All three carotids were ligated and excised with the tumor. Patient died one hour after the operation from hemorrhage and shock.

Case 29—Rivet (4.) Woman, 49 years old, had tumor opposite angle of jaw for seven years, but rapidity of growth had only been recent. At time of operation was size of egg. Diagnosis made of parotid tumor or aberrant goitre. Operation was followed by aphonia and for two or three weeks there was difficulty with deglutition. Recovery.

Case 30—Zondec (5.) Man, 63 years old. Had tumor on right side of neck for fourteen years. At time of operation tumor measured 7 x 5 cm. All three carotids tied at time of operation. Recovery.

Case 31—Coley and Downes (6). Man, 29 years old. Tumor in the neck of several years' duration. Size of hen's egg at time of operation. Diagnosis. Sarcoma of tonsil. External carotid ligated at time of operation, and hypoglossal nerve injured. Recovery after operation, but death one year later from recurrence.

Case 32—Author's case reported above.

Therefore in a total of thirty-two cases upon which operations were performed, we find eight deaths as the result of operation, an immediate mortality of 25 per cent., and six cases in which recurrence occurred. There were twenty cases in which all three carotids were tied and three in which the external carotid alone was ligated. And in addition to the nerve injuries as reported by Keen, as mentioned above, we must add one additional case each of injury to the hypoglossal, superior laryngeal, and facial nerves, together with three cases of post-operative paralysis of the vocal cord.

Because of the high mortality and the danger of injury to other important structures, Keen, in concluding his article, agrees with Reclus and Chevassu when he quotes: "Only rapid growth of an apparently malignant nature justifies operation."

A study of the reported cases, however, shows certain facts. The histories extend over a period of several years, in one case the growth being present for thirty-seven years, in others from four to twenty years. It would appear, then, that in the beginning these tumors are benign in their nature. But the history of the appearance of rapid increase in the rate of growth, the report of enlarged glands in six cases,

and of recurrence after operation in six cases, while one patient died of malignancy without operation, shows that a considerable number of those cases become malignant that were apparently benign in the beginning. And if one were to follow the conclusions of Reclus and Chevassu and of Keen and wait to operate until malignancy is apparent and the chance of recurrence greater, as well as the difficulty and seriousness of the operation increased, the prospect of cure is certainly not brilliant.

Moreover in but few of the cases reported was a correct diagnosis made before the operation, and it would appear that by calling attention to the existence of these tumors, an opportunity might be obtained of operating before they had attained a great size, and the operator knowing with what he had to deal could by free incision and careful dissection, and an accurate knowledge of the anatomy of the region, avoid injury to the nerves which in several cases has been one of the causes of the high mortality and disagreeable after-results of operation. Examination of the illustrations accompanying Keen's article shows that where the tumor has attained considerable size, its removal without ligation of the carotids would be impossible, but when the tumor is small it can often be removed without this additional risk.

In view of these facts, while recognizing that there may be a certain number of cases where a large but slowly growing tumor, without evidence of malignancy, exists in a patient whose age or whose general or arterial condition would make the danger of postoperative shock, or of brain disturbance after ligation of the carotids, especially great, in whom the operation would be inadvisable; it would appear to the writer that instead of advising against operation in all cases until rapid growth of malignancy occurs, more good could be accomplished by an effort at early diagnosis and removal of the tumor while the risk is less, and the prospect of lessened mortality and of an ultimate cure without recurrence greater.

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UNILATERAL LAMINECTOMY.*

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In December, 1908, while considering the resection of posterior spinal roots, the thought suggested itself that a procedure less extensive and bloody than the usual bilateral laminectomy would be desirable.

A series of trials upon the cadaver made it evident that ample room could be had by unilateral laminectomy, not only for resection of nerve roots within the spinal dura, but for many of the other purposes for which the spinal canal is opened.

So far as I know the operation is original, and was first done upon the living subject on December 16, 1908, in a case of Dr. T. P. Prout's. Since that time occasion has arisen to use the same technic upon various parts of the spine in four other cases (five in all).

The operation is as follows: The patient is placed face downward, sometimes flat, sometimes with the body slightly tilted to one side. In the five cases operated upon ether has been used. The incision is made just to one side of the spinal processes, and of sufficient length for the purpose in hand. The knife is carried close to the side of the spinous processes down to their bases. A broad deep retractor is used to pull the muscles outward (incidentally stopping hemorrhage) and the deeper layers of muscle are easily separated from the laminæ by a periosteal elevator. Gauze pads stuffed firmly into the wound and left for three minutes will give a dry field. When the pads are removed and the muscles well retracted, there are exposed the lateral surfaces of the spinal processes and the dorsal surfaces of the laminæ as far outward as the articular processes.

* Read before the New York Neurological Society, December 7, 1909.
Reprinted from Annals of Surgery, April, 1910.

Fig. 1.

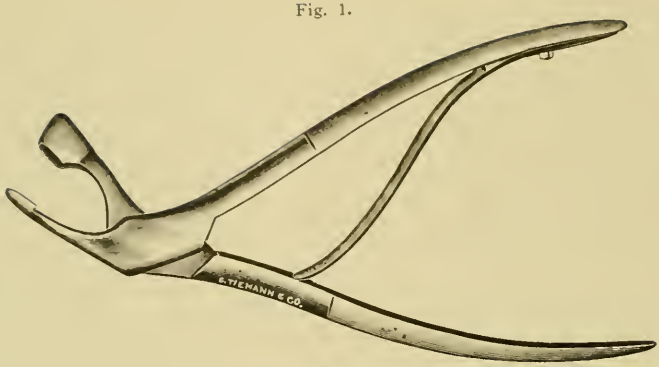


Fig. 2.

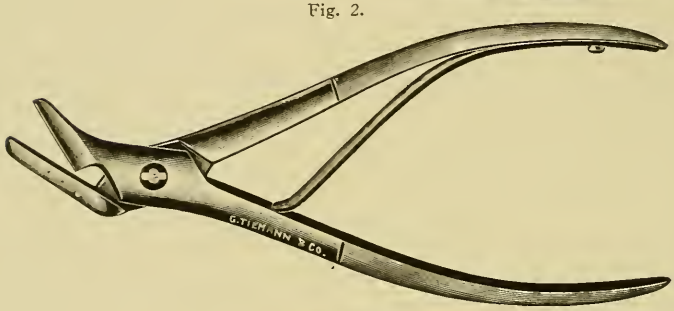


Fig. 3.

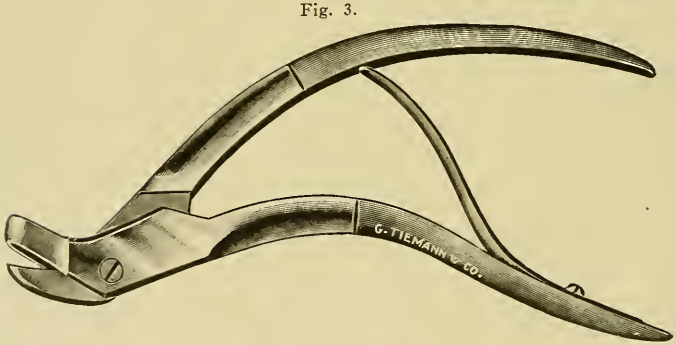
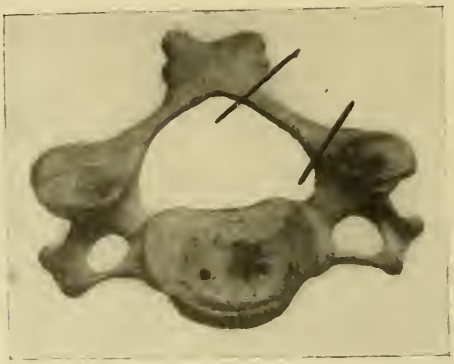


Fig. 5.

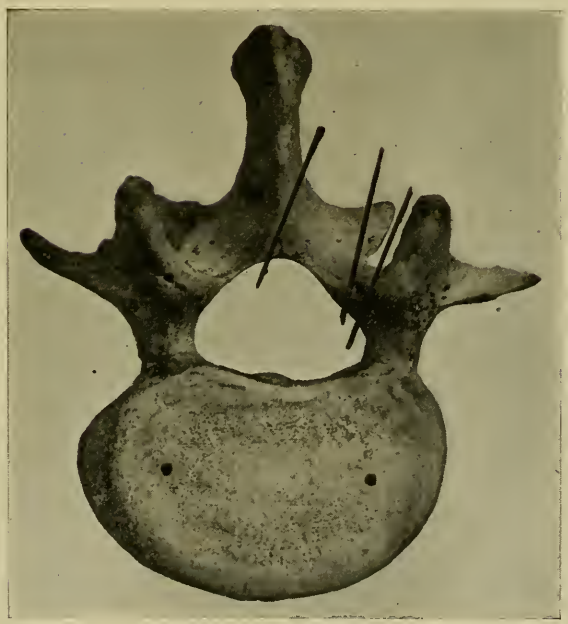


Fourth cervical vertebra.

Fig. 6.

Seventh dorsal vertebra.

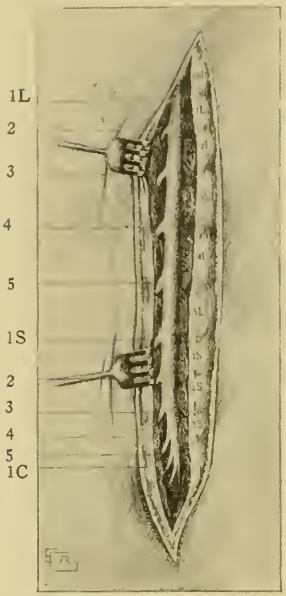
Fig. 7.



Third lumbar vertebra.

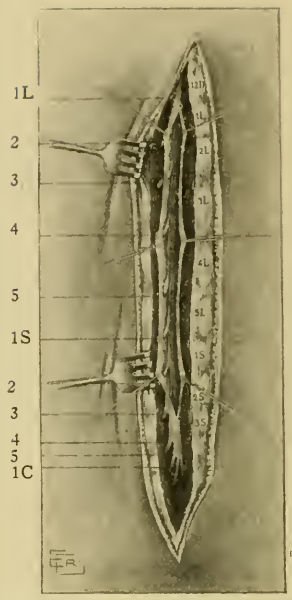
These vertebræ are life size, but come from a spinal column smaller than the average. The ink lines indicate the usual slant and position of the saw cuts. In Fig. 7 the outer cut is used when the articular process is sacrificed to gain more room. The laminæ in Figs. 6 and 7 are not so thick as they seem, because they are not photographed on edge.

Fig. 8.



Drawing from a dissection, showing unilateral laminectomy in the lumbar and sacral vertebræ. In this case the articular processes were encroached upon as in the outer line of section Fig. 7. The spines of the vertebræ are numbered on the right and the nerve roots on the left in the drawing. The artist has placed the roots a little too high to correspond properly with the spinous processes. The free view of the cord and the ease of exploring its lateral and anterior aspects is evident.

Fig. 9.



Same as Fig. 8, with the dura opened longitudinally. The same remarks apply to the relations of the roots to the spinous processes. Also the lower end of the cord itself should show at the level of the second lumbar spinous process. The cauda equina is easy to manipulate because of the length of its component bundles.

Fig. 10.

Fig. 11.

With a Doyen saw the laminæ are divided at their junction with the bases of the spinous processes, the line of section passing somewhat downward and inward (in the operating position). Another line of section is made well out toward the articular processes and is slanting like the preceding one (Figs. 5, 6 and 7). The laminæ vary in thickness in different parts of the spine, being thinnest in the cervical region, then increasingly thick downward through the dorsal and lumbar regions to the sacral region where they are as thin as in the cervical region (3 to 8 mm.). The saw has a guard by which the depth of the saw-line may be controlled. Moderate experience, however, teaches one to determine by the feel of the unguarded saw when it has divided the bone. This may seem a hazardous method, but the considerable fat layer surrounding the dura and the volume of the spinal fluid within the dura eliminate any real danger to the cord if the saw is handled with nicety. Hemorrhage has not been a factor in the cases so far done.

Fig. 12.

Case II. Boy, eight years old. Three months after operation. Figures 10, 11 and 12 show the postoperative flexibility of the spine. The laminæ removed lie between the ink marks. In Fig. 12 the dorsal linear scar shows faintly.

After the sawing is completed, a thin periosteal elevator is slipped beneath the lowest lamina which is raised sufficiently for a bone forceps to grasp and remove it, care always being used not to tilt the fragments so as to endanger the cord. The remaining laminæ are lifted out with the forceps.

In cases where only a small exposure is needed, one lamina may be removed by the use of the saw, and the remaining ones cut away with special rongeurs (Figs. 1, 2, and 3). This method does not give so advantageous an exposure for the exploration of the other side of the canal, because so favorable a slant at the base of the spinous process cannot be obtained with the forceps.

After removing the laminæ, the extradural layer of fat and veins is divided longitudinally in the middle of the wound, which is then gently packed with gauze to stop bleeding. After a few minutes the gauze is removed and the shiny dura is exposed in the bottom of the wound (Fig. 8).

The dura is divided longitudinally. First a short slit is made with a pointed knife, to let the spinal fluid, which spurts out, escape slowly. The division of the dura is completed with scissors, exposing the cord and nerve roots for whatever surgical attack is contemplated. Afterward the dura is closed with a continuous catgut

Fig. 13.

Fig. 14.

Case III. Boy, seventeen years old. Eleven days after operation. Figures 13 and 14 show the postoperative flexibility of the spine. The laminæ removed are indicated by the ink marks.

suture; the muscles are sutured to the interspinous tissues with chromic gut; the aponeurosis is closed with chromic gut; and the skin with silk.

No drainage is used. A firm sterile dressing is fastened by adhesive straps and a bandage. The patient lies mostly upon the sides or face during the healing process.

The exposure obtained by these methods varies in width with the portion of the spine involved. In the adult cadaver the following spaces were obtained: midcervical, 1¾ cm.; middorsal, 1 cm.; midlumbar, 1.3 cm. or even 1½ cm., by encroaching somewhat on the articular processes; midsacral, 1½ cm.

This approach admits the resection of the nerve roots on both sides of the cord without injury to the cord substance. This I have done upon the cadaver many times, and once upon the living subject, in the middorsal region.

In the region of the cauda equina it would be possible to anastomose motor roots of opposite sides.

In tumors of the cord this method gives an admirable exploratory approach. In many cases, I feel sure, there would be ample room for the removal of the tumor without further destruction of bone. With a large tumor, this method, by exposing its exact size and location, would enable the operator to remove just enough of the opposite laminæ for the easy extirpation of the tumor, and would thus minimize the loss of bony protection to the spinal cord.

This approach would almost certainly prevent the mishap reported in two cases by Dr. Joseph Fraenkel at the November meeting of this society, where the usual bilateral laminectomy failed to expose cord tumors which were found at autopsy to lie on the anterior aspect of the cord.

In unilateral laminectomy the side of the cord is well exposed and its anterior surface may readily be explored without injury to the cord substance (Figs. 8 and 9)

When the wound is completely sutured, the spinous processes are in their normal positions, there is no visible or palpable deformity of the back, and, because of the thick muscle pad overlying the laminæ, no form of examination, other than the X-ray, can determine the loss of bone. The cord, therefore suffers practically no loss of protection.

In all of the cases so far done (five in number) there has been little or no shock, primary union has resulted, and there has has been no loss of flexibility of the spine (Figs. 10 to 14 inclusive).

Much has been said of the dangers of allowing the spinal fluid to escape. In these cases it has escaped freely (6 to 12 ounces in different cases, estimated) and yet there has been little or no shock, and convalescence has been uneventful, so that the causes of the complications reported should, perhaps, be sought for elsewhere.

Systematic record of blood pressure, pulse and respiration during operation have not been kept. At the last operation Dr. Creevey noted that when the dura was first opened and the spinal fluid spurted out, there were one or two deep respirations, after which the breathing continued as before. There was no change in the pulse.

The neurological results in these cases will be reported at a later time by the neurologists for whom the operations were done.

The advantages of unilateral laminectomy are believed to be: Minimum loss of blood and of bone; and therefore minimum loss of bony protection to the cord. No postoperative deformity of the back or loss of flexibility of the spine. Exposure sufficient for all exploratory work except in certain cases of fracture of the spine: for all nerve root work on one or both sides; for the removal of many tumors, and for minimizing the operative trauma in others by first exposing their exact size and location. Exposure such as to diminish the chance of overlooking an anterior tumor.

THE TWO-STAGE PRINCIPLE IN OPERATIVE SURGERY.*

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Striving toward perfection in surgery, we must make every effort to master the art of operating; yet our final goal is always the security of the patient. Our motto might well stand:

"Not how skilful but how safe."

It is almost axiomatic that in technical skill practice indeed makes perfect. The axiom, however, is not always so evident in the matter of judgment, for here much

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depends upon individual powers of observation and upon the logical and judicial quality of the intellect which enables one to comprehend cause and effect. In following the course of a surgical disease with its multitude of complicated incidents the fitting together of related phenomena often enough becomes a task beyond the power of human mind.

Reviewing the causes of danger and of death in the operations of surgery we come upon three factors which are of paramount importance. These are the anæsthetic, the excessive loss of blood, and shock. Sepsis need not be here considered since, when directly due to the operation, it is after all a secondary and more avoidable source of peril; and when sepsis is present before the operation surgery is called in to overcome it.

We will first take up the matter of anæsthesia. It is quite certain that in spite of the utmost precaution a percentage of mortality is directly due to anæsthetic poisons. This is not denied by the most expert anæsthetists and, indeed, they are the very ones to sound the note of warning and to point out the necessity for care and experience in this branch of surgery. It follows, therefore, that in considering the dangers of any operation, the duration of anæsthesia as well as the variety and amount or dosage of the narcotic itself must be kept in mind. We must remember that the shorter the anæsthesia and the smaller the quantity of the drug used at one time the less will be the danger. If an operation promises to be of long duration, and if the saving of time is recognized as an important element, then we should consider the advisability of doing the work in two stages even though the total time of anæsthesia for the two stages be greater than that of the operation performed at one sitting. A quantity of narcotic may be taken with safety in divided doses which would surely prove lethal if taken at once.

Excessive Hemorrhage—The acute anæmia resulting from loss of blood at an operation is a frequent source of great danger and of death. It is best to avoid even the near approach of peril and, whenever possible, to stop the operation when hemorrhage causes the patient's condition to become alarming. The observation of the blood pressure is of much value and the warning of the sphygmomanometer should not be disregarded. Better surely operate twice or three times with safety than take unwarrantable risk in order to finish at one sitting the work and perhaps the patient.

Shock—Shock may be the result of hemorrhage, or it may be caused by manipulation of vital organs, or it may be the direct sequel of operations which have been unduly prolonged. Shock may be directly caused also by profound mental impressions attendant upon the scenes and experiences connected with operations even when performed without the aid of narcosis. Indeed, one of the the greatest boons of anæsthesia is the doing away with the psychical as well as the physical impressions upon the patient during the progress of surgical work.

Reasoning from the foregoing statements, the conclusion is inevitable that the cause of safety in surgery will be distinctly advanced, first, by using the smallest necessary amount of the anæsthetic; secondly, by avoiding excessive hemorrhage; thirdly, by shortening the actual time of operation.

For a number of years I have been convinced that one or another or all of these safeguards may be secured in certain operations by performing them in two or more stages. And, moreover, I would suggest that in planning any serious operation the possibility of the lessened risk by this method should be considered. When, for sound surgical reasons, the division of the operation has been decided upon, the wishes of the patient or his friends should be disregarded if a single-stage operation is urged in order to be through with a disagreeable experience. On one or two occasions I have regretted bitterly doing too much at one time, but I have never regretted dividing the operation.

I am well aware that many good surgeons will look with scorn upon this indication of apparent timidity, just as some regard the preliminary ligation of arteries as a confession of uncertainty in the technic of hæmostasis. What we are all working for, however, is to save the patient—to jeopardize him as little as possible. Often an operator will consider a procedure safe for one subject but not for another. Quite true. Then why be more reckless simply because the individual may seem capable of enduring an exceptional strain? The certainty of *preserving life* is the most important reason for the existence of surgery, though we are not unmindful of the other great branch, namely, to render life more desirable.

In some operations the two-stage principle has long been recognized—for example, in the older methods of performing cholecystostomy and colostomy. My plea, however, is for the more general acceptance of the doctrine in all operations which might be called extra hazardous and which, at the same time, lend themselves to a natural division into well-marked steps or stages. The tender-hearted person who could

not cut off the dog's tail at once but who managed to accomplish the result by removing an inch at a time may have multiplied pain in his feeble-minded endeavor, but he unconsciously subscribed to the theory well known to our forefathers in medicine, that the shock of an amputation increases in direct proportion to the proximity of the plane of section to the trunk of the individual.

In this paper I shall briefly discuss certain typical operations which appear to me particularly suitable for division into stages, but will not refer to those which from their very nature must occupy many sittings; such, for example, as complicated plastic work.

Operations Which Are Suitable for Division Into Two or More Stages.

1. For intracranial disease.
2. For intrapulmonary disease.
3. For obstruction of the bile passages.
4. For obstruction at the pylorus.
5. For malignant disease of the rectum.
6. For hypertrophy of the prostrate.
7. For suppuration of the kidney (nephrectomy).

Intracranial Operations—Hartley has pointed out that infection in operations upon the cranial contents occurs in direct proportion to the necessity for drainage. It would therefore seem that except in cases in which infection previously exists complete closure of the entire wound reduces the danger of sepsis. It follows that in operations for intracranial growths, for neurectomy and in similar procedures, completion of the operation in one stage promises the best results. It must, however, be recognized that some of these operations are accompanied by such profound shock as demonstrated by lowered blood pressure, whether due to hemorrhage or to interference with the vital centres, that completion of the operation signifies unwarrantable risk. If the work has been well planned, so that it may cease at any moment, the operation can be stopped, the wound *completely* closed and the patient sent back to bed to wait reestablishment of his equilibrium. A second or even a third sitting is then to be regarded as a separate operation. The danger is thus safely distributed so far as shock is concerned, although it is naturally doubled or trebled in regard to the more avoidable accident of sepsis.

Operations upon the Lungs—In the absence of apparatus for pneumatic differentiation, the extirpation of tumors of the lung and the evacuation of pulmonary abscesses, as well as cutting operations for the removal of foreign bodies, can be performed best by the two-stage method. The first step is for the purpose of accomplishing the local adhesion of visceral and parietal pleura, either by means of suture or by the formation of aseptic inflammatory exudate such as that following the application of zinc chloride solution to the unopened parietal pleura. The adhesion gives us a field for performing the pneumonotomy proper without the risk of the septic invasion of the entire pleural sac. And, indeed, it is probable that even with the help of apparatus for negative or positive pressure septic work on the lung will be less dangerous if the operation is divided. The pleura is extremely subject to acute spreading infections from very slight unsterile trauma. Then, too, we have here the added risk of pneumothorax.

Operations for the Relief of Biliary Obstructions—In prolonged icterus, especially when there are cirrhotic changes in the liver, even slight operative interference is apt to be followed by fatal recurrent or secondary hæmorrhagic oozing. To be sure, a few precautions may be taken to shorten the coagulation time of the blood,—such, for example, as the injection of alien serum before the operation. From personal experience, however, I am of the opinion that in operations of magnitude the danger of hemorrhage continues long after the good effects of the alien serum have disappeared. The safer mode of procedure, then, when deep chronic jaundice is present, is to employ serum or other therapy and to operate by the shortest and simplest possible method merely for the relief of cholæmia, reserving the removal of the cause of obstruction until a later operation.

My practice is to perform cholecystostomy for drainage and to do this in one stage through a small incision; and to avoid all unnecessary irritation of peritoneum whether by handling or packing. When the patient is in very poor general condition and when the obstruction partially yields after the cholecystostomy, as evidenced by the presence of bile in the stools, there is no reason whatever for hastening the second step. In the case of very old persons or those who have shown that they bear operations badly, it is best to continue biliary drainage indefinitely or even permanently.

For this purpose I use a little flexible solid rubber plug with a core of copper wire which permits the plug to retain any desired curve. At the distal extremity of the plug there is a thin pliable flange about two inches in diameter, which neatly adapts itself to the curve of the abdominal surface. About a half inch from the flange there is a bulbous enlargement of the stem which fits so firmly in the sinus itself that no bile or other discharge can escape. The diameter of the stem is about 14 to 16 French scale and the bulbous portion is two sizes larger. The total length of the appliance must depend upon the distance of the viscus to be drained from the abdominal wall—considerably greater in obese than in emaciated persons. The plug may be held in place by a strip of adhesive plaster and its presence is not a source of discomfort. It may be removed and cleansed once a day and in the event of a colicky attack due to closure of the cystic or common duct relief will be at once experienced on removal of the plug. I have patients who have been comfortable for years with simple drainage, preferring the condition to the dangers of a radical operation.

Pylorectomy—It appears to be pretty clearly proved that the safest method for performig this operation is by a combined extirpation of the pyloric region of the stomach and duodenum with complete closure of both open ends, followed by a gastro-enterostomy to act as an artificial pylorus.

It has been the custom to perform both these operations at one sitting. I would suggest, however, a plan which I have tested and will certainly make my rule, namely, to divide the operation. The advantages are several. The first and most important one is that in starved and emaciated persons the short and simple gastro-enterostomy is followed by an enormous improvement in the general nutrition and in strength, so that the pylorectomy itself becomes a far less shocking operation than it would have been without the preliminary step. Then, too, the second operation is often considerably shortened and is rendered easier by the subsidence of inflammatory thickening and adhesion about the neoplasm. I have seen a tumor the size of a large duck's egg disappear *completely* in the two weeks following gastro-enterostomy. At the second laparotomy the parts were carefully examined and not a trace of tumor or adhesion could be found, so the proposed pylorectomy was for the time abandoned, the patient being warned to report at once any symptoms of relapse. Naturally, this tumor could not have been neoplastic, but it was probably inflammatory due to the threatened perforation of an ulcer. If I had a similar case to treat I would remove the pylorus in any event.

Extirpation of Malignant Growth of Rectum—With preliminary colostomy for exclusion of the rectum the symptoms due to the continued functioning of the diseased organ are greatly ameliorated. Also the general condition of the individual thus relieved becomes so much improved that extirpation of the tumor or amputation of the rectum by any method becomes a good surgical risk, whereas before the colostomy the danger might have been prohibitive. At the same time, the preliminary abdominal section will afford a good opportunity for the examination of the upper limits of the neoplasm and the adjacent organs, so that the advisability of the radical operation as a further step can be determined. A year or two of life is far preferable, surgically speaking, to a death resulting from an attempted radical cure. I have more than once had occasion to note both the advantageousness of the preliminary colostomy and the unfortunate results of the attempted extirpation of an inoperable tumor without preliminary colostomy.

One case impressed me profoundly. It appeared to be a simple matter to remove a non-adherent tumor situated high in the rectum but demanding resection of the bowel. A laparotomy for colostomy revealed numerous unexpected metastases, some of which were in the liver—a condition which would have rendered any operation of greater magnitude a surgical crime.

Suprapubic Prostatectomy—It is not my purpose to enter here upon a discussion of the various routes of approach. My personal opinion is, as stated elsewhere, that the suprapubic is the preferable operation in the vast majority of instances. One of the most cogent reasons for advising this route is that it lends itself ideally to the two-stage operation. Even in the feeblest individuals the opening of the pneumatically distended bladder with the aid of local anæsthesia is an extremely short, simple and safe piece of work. We are then in a position to understand fully the exact conditions which cause the obstructive symptoms, and we may also explore, by sight if desired, the entire vesical wall including the ureteral and urethral orifices. Diverticula, tumors, and calculi—whether encysted or not—will be discovered. They may be dealt with at once or later, or not at all. Whether or not there is infection causing cystitis the troubles caused by the distressing periodic attempts to empty the bladder are done away with at once. Knowing that we are to have the opportunity

of this surgical and exact exploration it is unnecessary to do a preliminary cystoscopy, often in these cases a painful and even dangerous procedure.

Shock following cystostomy is extremely rare. The patient is out of bed the following day and may even be permitted to be upon his feet for a few minutes at a time. The second stage of the operation, enucleation of the prostatic growth, need not be undertaken until the patient's condition has so far improved that he can with reasonable certainty bear a general anæsthesia of from five to ten minutes.

Many of these patients being affected with arteriosclerosis are apt to bleed, and if the operation has been done in two stages great embarrassment may be avoided, since the surgeon will know the exact location of the hemorrhage. After the first stage this will be in the abdominal part of the wound. After the enucleation any bleeding which occurs will almost invariably come from the prostatic wound. When the work is done in one stage there are two places which may be expected to bleed, and the determination of the location of the hemorrhage is always troublesome, often difficult, and sometimes necessitates another anæsthesia—surely a disquieting and frequently a dangerous proceeding.

Should we be unfortunate enough to lose the patient after the cystotomy it is mathematically more probable that he would have succumbed after a cystotomy *plus prostatectomy.*

These are the most important advantages of the operation of suprapubic prostatectomy in two stages. All the good points of the suprapubic route need not here be enumerated.

Nephrectomy for Renal Suppuration—Removal of the kidney weeks or months after surgical drainage of the organ is usually difficult and dangerous because of dense adhesions to neighboring important structures. Indeed, secondary nephrectomy is so fraught with peril that many surgeons rate its mortality many per cent. higher than that of the primary form of the operation. Yet the removal of a large pus kidney with the flooding of the great flesh wound with enormous quantities of septic fluid is an extremely serious matter and is usually accompanied by great hazard.

Now, if we content ourselves with an ample incision for drainage and exploration, it will be noted that at the expiration of a week the sepsis will have become less severe, the tumor mass will have greatly diminished in size and nephrectomy may be quickly and easily performed, the entire operation consuming, say, from five to ten minutes. The adhesions, instead of being tough and fibrous, as they would have become with several weeks of delay, are succulent and easily separated with very little hemorrhage.

I have carefully tested this method and can report conscientiously that the danger of the double anæsthesia is not to be considered in comparision with the added factor of safety. Also, that there is a decided shortening of the total duration of the operation.

In conclusion, permit me to call your attention to two valuable points in operative surgery: First, arrange the operation whenever you can so as to permit cessation of the work at any moment. Second, get through with the essential part of the operation early, so that if you must stop the patient will have been relieved.